Functional outcome in people with diabetic neuropathy at four stages of foot complications

Candidate: **Rajani V Kanade**, Dept of Physiotherapy

Supervisors: **Dr. Robert van Deursen**, Dept of Physiotherapy

Prof. Patricia Price, Wound Healing and Research Unit

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PhD

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Summary

Background:

This study was designed to investigate the nature of the course of functional outcome across the four patient groups with diabetic neuropathy at consequent stages of foot complications namely: diabetic neuropathy without history of plantar ulceration (DMPN), active plantar ulceration (DFU), healed unilateral partial foot amputations (PFA) and healed unilateral trans-tibial amputations (TTA). The secondary objective was to compare the functional outcome between patients with DFU and PFA and patients with PFA and TTA.

Methods:

In this cross-sectional case control study, 4 matched groups of patients with DMPN were studied: DMPN (n=23); DFU (n=23); PFA (n=16) and TTA (n=22). Appropriate outcome measures were used to evaluate function in 3 domains, namely Mobility and its impact on weight-bearing (sit-to-stand, standing balance, gait and plantar pressures during walking), Level of Activity (capacity and performance of walking) and H-RQOL.

One–way ANOVA was used to compare 4 groups and linear polynomial contrast detected the trend across groups. In cases of significant difference between the 4 groups, an Independent sample t-test was used for specific group comparison.

Results:

There was a significant difference in functional outcome between the four groups demonstrating an overall decline in the level of function with the progression of impairment (standing balance: $p=0.002$, gait velocity: $p<0.001$, daily strides: $p<0.001$, SF-36 Physical function: $p<0.001$). The risk of plantar injury to the entire affected foot during walking increased from DMPN to DFU to PFA ($p=0.013$).

There was no significant difference between the overall function of DFU and PFA. The PFA and TTA groups also varied significantly only in the domain of activity performance wherein the TTA group demonstrated a low daily walking performance compared to the PFA group ($p=0.006$).

Conclusion:

The overall decline demonstrated in this study in the three domains of function with progression of physical impairment from the DMPN to TTA group, calls for an urgent need to define a tailormade rehabilitation programme to maximise function of these patient groups. The increasing risk of plantar injury from DMPN to DFU to PFA during walking warrants a greater and precise focus on footcare of the affected as well as the contra-lateral foot.

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List of Abbreviations

COG: centre of gravity

COP: centre of pressure

CWIS: Cardiff Wound Impact Scale

DFU: Diabetic foot ulcer

DMPN group: Group with diabetic neuropathy alone

DMPN: Diabetic neuropathy

DPCS: daily plantar cumulative stress

H-RQOL: health related quality of life

ICF: International Classification of Function

LEA: lower extremity amputation

MPP: maximum peak pressure

MT: metatarsal

MTP: metatarso-phalangeal

PFA: partial foot amputation

PTI: pressure time integral

RMI: Rivermead Mobility Index

ROM: range of motion

SAM: step activity monitor

STS: sit-to-stand

S-W monofilaments: Semmes Weinstein monofilaments

THBI: Total Heart Beat index

TTA: trans-tibial amputation

1-2 MTP: first and second MTP

3-4-5/3-5 MTP: third, fourth and fifth MTP

Glossary of terms

Centre of pressure: The point of application of GRF.

Ground reaction force: The force reflected back up into the feet through the same action line with the same magnitude in response to the weight of the person standing is termed as GRF.

Moment: A turning or rotatory effect produced by the application of a force / A rotational potential of the forces acting on the joint.

Muscle moment: is the product of the force within the muscle and the distance between the line of action of the muscle and the axis of rotation of the joint.

Net joint moment: Sum of the net action of the muscles and the inherent tension in ligaments around a joint.

Units:

1 stride= right step + left step i.e. 2 steps

Cadence= steps/min

Chapter 1: Introduction

Diabetes mellitus (DM) is the global epidemic of the 21st century and now the fourth leading cause of death in most developed countries (International Diabetes Federation and International Working Group on the Diabetic Foot 2005). In the year 2000, World Health Organisation (WHO) reported the prevalence of diabetes in the United Kingdom of Great Britain and Northern Ireland as 1,765,000 and it is estimated to be 2,668,000 by the year 2030, which is almost twice the existing numbers (WHO European region 2005). It is a serious chronic disease with multi system involvement. Apart from the various complications such as nephropathy, retinopathy and cardio-vascular disorders, foot complications secondary to peripheral neuropathy are a major cause of mortality and morbidity in the diabetic population (Rayman et al. 2004).

Diabetic peripheral neuropathy (DMPN) is a common complication affecting approximately 50% of the diabetic population (Pirart 1977, Reiber et al. 1999). It is the major aetiological component of most foot ulcerations (Boyko et al. 1999, Reiber et al. 1999). Approximately 15% of diabetic people develop foot ulceration (International Diabetes Federation and International Working Group on the Diabetic Foot 2005). The annual incidence of foot ulceration is 6.3 % in diabetic neuropathic patients whereas it is 0.5% in diabetic patients without DMPN matched for age, gender and DM duration (McGill, Molyneaux & Yue 2005). Foot ulcers are known to deteriorate to deep infection or gangrene precipitating more than 85% of amputations in those with diabetes (Apelqvist & Larsson 2000). In an attempt to salvage the foot for ambulation, partial foot amputation (PFA) is often performed (Hosch et al. 1997). PFA often predispose the diabetic patients to increased foot pressures and development of foot deformities, which further increases their risk for ulceration and amputation (Armstrong et al. 1997). Hence, DMPN is known to show a progressive course with limb amputation as the final end-point of the disease (Sima & Greene 1995). However, a single limb amputation does not appear to mark the ultimate end of the progression of events in diabetic foot complications.

Thirty percent of diabetic people undergoing single leg amputation require an amputation of the remaining limb within 3 years, and the figure rises to 51% in 5 years (Most & Sinnock 1983). One of the aims of the St. Vincent declaration was to reduce lower extremity amputations (LEA) related to diabetes mellitus by one half within 5 years (1989), however data suggest these targets have not been met (Stiegler et al. 1998). Between 41% and 70% of diabetic people who have undergone a leg amputation, do not survive more than 5 years after the surgery (Most & Sinnock 1983). A recent report from International Diabetes Federation and International Working Group on the Diabetic Foot (2005) suggests a further disconcerting rise in the mortality rate in diabetic people following LEA. Ten percent of patients die around the time of amputation, 30% of people who have undergone amputation die within one year, 50% die within three years and 70% die within five years. Apart from the high mortality rate following amputations in people with DM, diabetic amputations also result in high morbidity and an economic burden to the health care systems (Apelqvist & Larsson 2000).

Generally, the costs of diabetes mellitus are either direct (including medical care costs to the individual and the family, hospital care costs for the treatment of complications) or indirect (including sickness, absence from work, disability, premature retirement or premature mortality affecting the productivity) or intangible costs [including pain, anxiety, inconvenience & other factors which can reduce the Health-related quality of life (H-R QOL) or affect it negatively] (WHO, 2005). Despite the devastating impact of diabetic foot complications on morbidity and mortality, the functional outcome of these people is still unclear. Functional outcome can be interpreted as the capacity and performance of activities of daily living and participation of an individual in daily life (ICF 2002).

The review of literature presented in the subsequent chapter will suggest that attempts to evaluate functional outcome of patients with diabetic foot complications fail to identify the specific problem areas in these domains of function. Apart from the fact that it may appear that physical impairment of the diabetic neuropathic patients increases with further foot complications, very little is known about the actual impact of these complications on functional outcome. It is therefore believed that a comprehensive evaluation of functional outcome will provide an insight into the capacity, performance and participation in daily life of diabetic patients in the presence of foot complications.

Therefore, it is proposed to evaluate foot function with a model, which shadows the ICF model of function (ICF 2002). However, the ICF model cannot be applied in its present total form to address the research question of this study. ICF is primarily designed to find a role in the planning and implementation of health care services (ICF 2002) and therefore when the concept of function is applied to the research sector it needs to be approached with a combination of clinical relevance and scientific investigation.

A clear understanding of the problem areas can guide the clinical services to plan purposeful management strategies to optimise functional outcome in these patients. Considering the multi-system involvement of DM, it would be very difficult to speculate on the beneficial effect of improved function on the mortality rate following serious diabetic foot complications. However, it would be reasonable to expect a reduction in the morbidity associated with foot complications in diabetic people resulting in better functional outcome. There is already an increased recognition among social planners and service agencies that reductions in the incidence and severity of disability in a population can be brought about by enhancing the functional capacity of the person and by improving performance by modifying features of the social and physical environment (ICF 2002).

Concurrently the shift of paradigm of the WHO from merely 'life expectancy' to 'healthy life expectancy' (McArdle, Katch, & Katch 2001) emphasises the need for such a perspective. Life expectancy estimates determine the overall length of life based on mortality data without considering the quality of life as ageing progresses, whereas the concept of 'healthy life expectancy' deals with the expected number of years a person might live in the equivalent of full health (McArdle, Katch, & Katch 2001). Findings from a comprehensive model of functional outcome may reflect the full health of an individual and ultimately assist in estimating healthy life expectancy. Apart from estimating the functional health of an individual, functional status information has also found a role in care planning, measurement of quality of care and adjustment of payments for case mix under various Medicare prospective payment systems in countries like USA (Carter et al. 2003). Considering the value of the functional status information in health planning and management, a comprehensive evaluation of functional outcome in a chronic condition such as diabetic foot complication is deemed essential.

Therefore, the objective of this study was to explore the functional outcome in patients with diabetic neuropathy at four consequent stages of foot complications namely diabetic neuropathy (DMPN), plantar ulceration (DFU), partial foot amputations (PFA) and trans-tibial amputations (TTA). The primary objective was:

1. To investigate the nature of the course of functional outcome across the four groups.

The secondary objectives were:

2. To compare the functional outcome between the DFU group and the PFA group.
3. To compare the functional outcome between the PFA and the TTA group.

Chapter 2: Literature review

The purpose of the literature review for the present study was to provide an overview of the prevailing concept of foot function in patients with various musculo-skeletal disorders and focus on functional outcome in the presence of diabetic neuropathy at different stages of complications i.e. plantar ulceration, partial foot amputations and trans-tibial amputation.

A thorough literature search was conducted using ISI Web of Science (SCI-EXPANDED, SSCI, A & HCI), Ovid MEDLINE, AMED (Allied and Complementary Medicine), CINAHL (Cumulative Index to Nursing to Nursing & Allied Health Literature), EMBASE, Your Journals @ Ovid, EBM Reviews (Cochrane Central Register of Controlled trials), EBM Reviews (ACP Journal Club), EBM Reviews (Database of abstracts of Reviews of Effects). The keywords used included- foot function/functional outcome, diabetic neuropathy, plantar ulceration, partial foot amputations and trans-tibial/below-knee amputations. The search strategy began with individual key words and then they were used in different combinations to focus the search on foot function. The results from the search strategy are presented in Table 2.1. In total 615 records were found between all the above mentioned databases. However, the overlap between the results of the databases was over 90%. Effectively 39 records related to foot function/lower limb function/ functional outcome in patients with or without DMPN, DFU, PFA and TTA were identified from the databases to discuss the function of the foot. These records were considered to be relevant to the topic of review since they were related to functional outcome or impact of a foot disorder on the patients in general or in terms of H-RQOL. Additionally, references relevant to the topic which were not located by the electronic search were traced by hand search through the route of cross-references. The records included were based on case-control studies, literature reviews, exploratory studies, theoretical evidence from textbooks and reports of WHO.

Table 2.1: Search strategy adopted for literature search

Database	Time duration	Total number of records	Relevant records
ISI Web of Science-SCI-EXPANDED, SSCI, A & HCI	1970 to 2005	145	**28**
Ovid MEDLINE	1966 to 2nd week Feb 2006	146	**21** (including 3 new compared to ISI)
AMED (Allied and Complementary medicine)	1985 to Feb 2006	74	**18** (including 3 new compared to ISI & MEDLINE)
CINAHL-Cumulative Index to Nursing to Nursing & Allied Health Literature	1982 to 2nd week Feb 2006	65	**11** (including1 new compared to ISI , MEDLINE & AMED
EMBASE	1980 to 7th week 2006	134	**28** (including 1 new compared to ISI , MEDLINE & AMED & CINAHL)
Your Journals @ Ovid		32	**3** (all new articles)
EBM Reviews- Cochrane Central Register of Controlled trials	1st quarter 2006	16	**7** (no new articles)
EBM Reviews - Cochrane Database of Systematic Reviews	1st quarter 2006	3	**0**
EBM Reviews- ACP Journal Club	1991 to Jan/Feb 2006	0	**N/A**
EBM Reviews- Database of abstracts of Reviews of Effects	1st quarter 2006	0	**N/A**

N/A: Not applicable

2.1: Broad concept of 'Function':

The exploration of foot function begins with the definition of 'Function'. The term function has assumed numerous and diverse meanings in the health literature (Jette 1985). This term is commonly used to describe either the (a) characteristic action of body parts, e.g. function of the shoulder (b) performance of organs, e.g. kidney function or (c) performance of the individual, e.g. functioning in activities of daily living (ADL) (Jette 1985).

The literal meaning of the word 'Function' described by the Oxford dictionary is an activity that is natural to or the purpose of a person or thing (Soanes, Waite & Hawker 2001). A review of existing literature in this field indicates that the function of the foot has been either interpreted as a univariate component, largely based on impairment or the biomechanical model of the joint complex or it has been measured with self-reported instruments alone (Budimanmak, Conrad & Roach 1991, Perry 1992, Siegel et al. 1995, Garbalosa et al. 1996, Kemler & De Vet 2000 & Kirby 2001).

Overall, the interpretation of the term function has been largely restricted to the sensory-motor performance of the foot complex (Garbalosa et al. 1996, Bertani et al. 1999, Kemler & De Vet 2000). Some studies have measured foot function in terms of the results obtained from gait analysis and plantar pressure distribution (Woodburn et al. 2003, Thometz et al. 2005 & Hallemans et al. 2006). However, with the advent of the International Classification of Function (ICF 2002), function is gaining a wider perspective in the context of health and health-related domains. In ICF, the term 'functioning' refers to all body functions, activities and participation in daily living. The three levels of human functioning classified by ICF are functioning at the level of

(1) the body or body part, (2) the whole person and (3) the whole person in a social context (ICF 2002). Prior to proposing a comprehensive model for evaluation of functional outcome in patients with diabetic foot complications the existing models of function are discussed.

2.2: Existing models of foot function:

The concept of foot function is not new to the field of rehabilitation science. There is a broad spectrum of definitions to describe foot function largely based on individual theory or logic (Hughes & Klenerman 1985, BudimanMak, Conrad & Roach 1991, Knopp et al. 1993, Garbalosa 1996, Gorter, Kuyvenhoven & de Melker 2000, Kemler & De Vet 2000 & Kirby 2001). Effectively there is no consensus in the method of assessment resulting in a battery of both performance-based and self-reported instruments to measure function.

Objective assessment of the biomechanical parameters of the ankle-foot complex has been conventionally used to measure foot function.

To begin with, Katoh et al. (1983) examined the temporal and distance related gait factors, foot-switch contact patterns, ankle/subtalar joint motion and centre of foot pressure distribution with the objective of biomechanical analysis of foot function during gait (Katoh et al. 1983). Based on their findings from 13 patients with complaints of heel pain compared with 41 normal subjects, the authors concluded that the potential applications of biomechanical assessment of gait are promising. The specific effect of a pathological process on a given parameter (among the parameters described above by the authors) can assist in making a diagnosis. Moreover, application of this information can be extended to suggest various treatment goals or rationales.

Almost a decade later Perry (1992) interpreted the function of the foot based on its motion and muscular control to relate to three events: shock absorption, weight-bearing stability and progression during gait cycle in her textbook (Perry 1992).
Around the same time, Siegel et al. (1995) described another technique to measure foot function during the stance phase of gait, which allowed variables such as ground reaction forces and centre of pressure location to be expressed in a local foot coordinate system to give more anatomical meaning to the interpretation of results (Siegel et al. 1995). Six subjects (1 subject without foot pathology, 4 subjects with rheumatoid arthritis (RA) and 1 subject with an excessively pronated foot) were studied and foot function was evaluated with a 3D computerized movement analysis system. Based on the findings the authors concluded that for the foot problems presented, the resolution and the accuracy of the evaluation technique and selection of appropriate output variables appeared sufficient to distinguish normal from pathological function and to discriminate between various levels of impairment.

Later on Kirby (2001) proposed a theory of foot function based on the spatial location of the sub-talar joint axis in relation to the weight bearing structures of the plantar foot. This theory explained how externally generated forces, such as ground reaction force and internally generated forces, such as ligamentous and tendon tensile forces and joint compression forces affect the mechanical behaviour of the foot and lower extremity (Kirby 2001).

Another study reported the benefits of using instrumented gait analysis to evaluate foot function in the case study of a patient with rheumatoid arthritis (RA) following forefoot reconstruction (Turner, Davys & Woodburn 2005). The authors adopted a comprehensive approach to instrumented gait analysis including foot motion, spatio-temporal parameters of gait and foot pressure distribution to inform foot function. The potential benefits of gait analysis for better understanding of foot structure and function were highlighted in this study. The approach adopted in this study can be described as a comprehensive approach to instrumented gait analysis. However it fails to explain how gait analysis alone can inform complete foot function, thereby lacking the conceptual framework underlying gait analysis to evaluate foot function. Two more studies were located, which used gait analysis to determine foot function in patients with rheumatoid arthritis and in patients following subtalar distraction bone-block arthrodesis (Woodburn et al. 2003, Rammelt et al. 2004).

Woodburn et al. (2003) studied RA patients (n=23) with painful pes planovalgus deformity to compare their gait and foot function with age and sex matched adults (n=23). Gait analysis measurements included the temporal and spatial parameters of gait and plantar pressures and 3D kinematics at the ankle joint complex during walking. This was an elaborate study, which concluded that painful pes planovalgus deformity in RA is associated with global changes in gait, and localised structural and functional changes in the foot, which can be accurately, measured using clinical gait analysis. Such valuable information is crucial in the logical planning of the appropriate disease staged interventions as pointed out by the authors. However, it is unclear from the report as to how the authors defined foot function. Whether gait analysis is a part of foot function evaluation does not receive any attention in this report. Therefore, the description of the concept of foot function in their study limits the value of this approach of foot function evaluation.

Rammelt et al. (2004) evaluated foot function based on dynamic pedobarography and clinical assessment. Clinical evaluation included the American Orthopaedic Foot and Ankle Society (AOFAS) hindfoot scale, radiological evaluation and modified Bargon scale to assess the various components of the ankle-foot complex. Even this study provided detailed information regarding the mechanics of the ankle-foot complex during walking before and after arthrodesis, which will be useful in the clinical management of these patients. However, there is no description of the concept of foot function and why the authors thought that the chosen outcome measures would inform foot function comprehensively (Rammelt et al. 2004).

Recently Hallemans (2006) described foot-contact patterns, oscillations of the centre of pressure (COP), peak pressures, relative vertical impulses and foot shape indices as foot function parameters to monitor changes in foot loading during the first 5 months after the onset of independent walking in toddlers (Hallemans et al. 2006). Ten toddlers were studied at 1, 2, 3, 4, 6, 8, 10, 12, 16 and 20 weeks after the onset of independent walking to describe the foot function parameters.

All these studies provide valuable information for understanding the normal and the altered mechanics of the foot during walking in the presence of musculo-skeletal disorders and have the potential to confirm the diagnosis and guide the treatment process. However, they represent diverse singular concepts of foot function, which makes it difficult for a researcher to choose a single approach to evaluate function. Moreover, they fail to inform several other aspects of the physical dimension of function related to the foot function such as the ability to perform common tasks of mobility e.g. sit to stand (STS) transfer, balance in an upright posture and daily walking performance.

Furthermore, not all the approaches mentioned above were developed to measure foot function based on the evidence from research. Some of the concepts are largely based on the theoretical reasoning of the researchers. Although the theoretical framework is essential in interpreting the term function or functional outcome following foot complications it is hard to accept the descriptive models of function without underpinning them with evidence based on research studies powered to detect differences in functional outcome (based on the outcome measures used).

Apart from gait analysis, several studies have reported the measurement of foot function using plantar pressure distribution in a wide range of musculo-skeletal conditions. Thometz et al. (2005) correlated radiographic measurements to the dynamic plantar pressure of the residual clubfoot by comparing radiographs and EMED plantar pressure results in 61 idiopathic clubfeet in 39 children at an average of 8 years after complete subtalar release (Thometz, Liu, Tassone & Klein 2005). They concluded that radiographs used in concert with dynamic plantar pressure analysis will provide a more complete assessment of the corrected clubfoot and equated this approach of foot assessment to foot function.

Another study evaluated foot function solely in terms of plantar pressure distribution. Four patients with malignant tumors of the proximal toe phalanx treated with ray resection and reconstruction by free microvascular fibula transfer, intermetatarsal

bony fusion, or soft-tissue stabilization were studied and followed up between 21 months and 8 years. The study demonstrated that the patients showed normal gait (determined based on plantar pressure distribution) and remained relapse free during the follow-up period (Ramseier, Jacob & Exner 2004).
Yet another study examined 27 subjects while wearing modified Root and Blake style orthoses with an in-shoe pressure measurement system. The authors noted that significant changes were observed in the temporal parameters of gait and the loading pattern of the foot was altered when subjects wore the orthoses (Reed & Bennett 2001).

Rosenbaum et al. (1997) used peroneal reaction time measurements elicited on a rapidly tilting platform (recorded with surface electromyography) in addition to the pressure distribution measurements during walking to measure foot function following modified Evans repair for chronic ankle instability (Rosenbaum et al. 1997). Nineteen patients were studied at a 10-year follow-up. The authors concluded that the persistent clinical problems as well as the functional changes following modified Evans repair indicate that the disturbed ankle joint kinematics permanently alter foot function and may subsequently support the development of arthrosis. Therefore, the procedure should be used judiciously in patients with chronic ankle stability. Functional changes were described in terms of reduced peak pressures under the lateral heel and increased pressures under the longitudinal arch and shorter reaction times of the peroneal muscles on the operated side.

Particularly the measurement of centre of pressure has been widely used in the evaluation of foot function (Fuller 1999). Fuller (1999) described the centre of pressure and indicated how it can be used to calculate moments about the joint axes of the foot. The researchers proposed a model based on the use of the location of centre of pressure relative to the location of the subtalar joint axis for theoretical explanation of selected foot pathologies and their treatment.

The above-described studies provide useful information regarding the alteration of foot loading during gait based on the plantar pressure distribution. The work is commendable in terms of the innovative approaches developed to understand the pathomechanics of the foot during walking based on the plantar pressure distribution. Moreover, some of the studies have a substantial follow-up period to monitor the changes in function over time. However, it needs to be highlighted that plantar pressures during gait alone cannot be equated to complete assessment of foot function.

Foot function has also been measured in terms of joint deformities and post-burn contractures / deformities in children with severe foot burns (Shakirov 2005). Such an approach is also a singular approach, which accounts for joint mobility alone and overlooks the remaining aspects of foot function.

In addition to the tools described above for the measurement of foot function in terms of biomechanical analysis of gait, plantar pressure distribution and joint mobility, specific performance and self-administered tests have been described in the literature to assess foot function.

A foot function index (FFI) was developed to measure the impact of foot pathology on function in terms of pain, disability and activity restriction. The FFI is a self-administered index consisting of 23 items divided into 3 subscales: foot pain, disability and activity limitation. The index is shown to have good test-retest properties (ICC for Pain=0.695, Disability=0.84, Activity limitation=0.81, Total score=0.87) and also adequate construct and criterion validity. The authors anticipate that the FFI could be applied to non-RA subjects with foot pain, though they themselves tested on subjects with foot pain resulting from RA (BudimanMak, Conrad & Roach 1991).

However, this index being a truly self-reported measure does not have the potential to assess the actual performance of the foot in the activities of daily living (ADL). Moreover, the FFI appears to be a reasonable tool for individuals with foot disorders with low levels of function. It may not be appropriate for individuals who function at or above the level of independent activities of daily living (Agel et al. 2005). It is also doubtful whether FFI is sensitive to clinical change (Soohoo et al. 2006).

Foot Health Status Questionnaire is another foot specific questionnaire specifically designed to measure foot health related quality of life. It was primarily developed to assess subjects undergoing surgical treatment for common foot problems. However, it was validated across a wide spectrum of pathologies including skin, nail and musculo-skeletal disorders. The authors claim that it can be used to evaluate the level of effectiveness of clinical interventions (Bennett & Patterson 1998). It is a psychometrically evaluated questionnaire that contains 13 items covering foot pain, foot function, footwear, and general foot health. The tool demonstrates a high degree of content, criterion, and constructs validity and test-retest reliability (ICCs ranging from 0.74 to 0.92) (Bennett et al. 1998). However even this tool has a major limitation of being a self-reported measure which fails to provide objective information about the performance of the patients with foot complications.

Comparison of the two foot-specific HRQOL questionnaires: the Foot Function Index (FFI) and the Foot Health Status Questionnaire (FHSQ) in patients with plantar fascitis revealed that the FFI is generally less responsive to change, particularly in the domain of Activity Limitation. The authors confirmed that the FHSQ has several advantages when evaluating HRQOL in patients being treated with foot orthoses for plantar fasciitis, and should be viewed as the preferred questionnaire (Landorf & Keenan 2002). It is necessary to emphasise at this point that 'function', 'health status' and 'H-RQOL' are not interchangeable terms. Therefore, researchers should be cautious with the application of the FHSQ to evaluate H-RQOL in patients with foot disorders. Furthermore being a truly self-reported measure even FHSQ has limitations in assessing the actual performance of the foot in the activities of daily living as, a self-reported measure may only be a surrogate measure of evaluating the actual performance of the patient in the presence of foot disorders.

A couple of years later an objective and standardised test of foot function came into existence to assess the actual performance of the patients with foot complications. Kemler & De Vet 2000 developed a test of foot function performed in a seated position to evaluate several basic aspects of individual foot function (Kemler & De Vet 2000). Normative values were obtained for 100 healthy patients between 20 and 70 years of age. The test was further validated on 20 patients diagnosed with reflex sympathetic dystrophy of one foot. Four subsets were chosen to provide a broad sampling of foot function: 1) Forward and Backward Shifting (FBS) of a foot panel to

measure mobility, 2) Lateral Shifting (LS) of a foot panel to measure mobility, 3) Alternately touching two bells (TB) to measure coordination and mobility &
4) Depressing a pedal (DP) to measure strength and mobility. The intrarater and interrater reliabilities of the test were high (eg. intrarater correlation coefficient ranged from 0.74 to 0.93 and inter-rater from 0.85 to 0.99). The authors claim this test is a simple, convenient and reliable device for the objective assessment of foot function applicable to non-ambulant patients. Albeit this test was designed to evaluate function of the foot among non-ambulant people, it obviously fails to provide information on the role of weight bearing of the foot thereby making it inappropriate for evaluation of foot function in the present study. Furthermore it lacks the ability to examine the role of the foot in the most commonly performed activities of daily life which are weight-bearing activities (STS transfer and walking) to inform a comprehensive picture of foot function.

Most recently a new scale has been developed to assess foot status in rheumatoid arthritis (RA) using qualitative methodology and item response techniques (Rasch analysis) (Helliwell et al. 2005). Although the Foot Impact Scale was not labelled as a foot function scale, the scale was developed to assess the impact of RA and to measure the effect of interventions developed. The 51-item questionnaire included two subscales, which covered the domains of impairment/shoes and activities/participation, which is parallel to the domains of function described by the International Classification of Function (ICF 2002). Both the subscales demonstrated good psychometric properties, external validity and test-retest reliability. Therefore, such a disease specific scale demonstrates an excellent example of a comprehensive instrument for the assessment of the impact of the disease in patients with RA.

However, it has a major limitation of being exclusively a self-reported measure and a disease specific tool applicable for patients with RA.

In a parallel context, it has already been identified that physical activity questionnaires allow researchers to sample large populations with relative ease but they rely on the patient's ability to perceive and estimate their own performance, which may be more or less than their actual performance (Bassett, Cureton & Ainsworth 2000). Similarly, the Foot Impact Scale can be considered as an excellent tool to assess the impact of RA in a large patient population however, objective tools designed to identify and quantify the specific problem areas are necessary for detailed comprehensive evaluation.

These different approaches clearly indicate that foot function has been interpreted singularly, either in terms of various biomechanical models of the foot or based on a performance test which is designed to assess mobility, co-ordination and strength in the seating position or based on a self-reported measure. Perry's (1992) interpretation has extended the furthest to evaluate the three major components of foot function in the order of hierarchy of events during gait cycle however it is limited to the motion and the muscular control of the foot. Recently the approach adopted by Turner et al. (2005) for the evaluation of foot function was quite comprehensive. The purpose of such a comprehensive analysis was to use the valuable information in clinical decision making in a multidisciplinary team however, the focus of evaluation of foot function was on instrumented gait analysis and it lacked the conceptual framework underlying it. The most recent approach implemented by Helliwell et al. (2005) appeared to represent a comprehensive tool for assessment of functional outcome in patients with foot complications. However, it is limited in being a disease specific tool applicable for patients with RA and moreover it is a self-reported measure which lacks the ability to measure the actual performance of the patient. It is clear that the self-reported tests and performance-based tests measure two different constructs of function and therefore should be treated as complementary measures for comprehensive evaluation of function as against substituting one with another.

Therefore although all the tools described above can be used to measure foot function they are limited in providing information exclusive to the domain or the aspect of function assessed by them. Hence, solitary application of any one tool is inadequate to inform a comprehensive picture of foot function.

Further to the review of literature describing the tools of assessment of foot function in a wide range of foot disorders, the chapter continues to discuss the various approaches of assessment of foot function at consequent stages of diabetic foot complications.

2.3: Functional outcome in the presence of longitudinal complications of the foot following diabetic neuropathy:

Several studies have investigated sensory-motor impairments (Johnson, Doll & Cromey 1986, Arkkila, Kantola & Viikari 1994, Muona & Peltonen 1994, Sima & Greene 1995), biomechanical changes (Cavanagh et al. 1997, Payne 1998, Caselli et al. 2002), standing balance (Boucher et al. 1995, Uccioli et al. 1995, Katoulis et al. 1997, van Deursen & Simoneau 1999), gait characteristics (Cavanagh et al. 1992, Courtemanche et al. 1996, Katoulis et al. 1997, Walker, Helm & Lavery 1997, Menz et al. 2004), plantar pressure distribution (Stess, Jensen & Mirmiran 1997, Frykberg et al. 1998, Lobmann et al. 2002, Payne, Turner & Miller 2002) and daily walking activity following DMPN (Tudor-Locke et al. 2002). However, there is no evidence from the literature to suggest any attempts to investigate the functional outcome when the diabetic foot is at the stage of peripheral neuropathy although it is evident (from the work cited in this paragraph) that several researchers have assessed different aspects of function singularly without designing the studies specifically for functional evaluation. This may be the case because in most cases, diabetic foot complications are seen as wounds subsequent to trauma and less often as an acute neuroarthropathy or cellulitis without any apparent skin lesion (Got 2001).

The neuro-physiological changes occurring due to DMPN in the alteration of foot function cannot be underestimated. It needs no further emphasis that balance and postural control relies upon the integrity of peripheral sensory information (Woollacott, Shumwaycook & Nashner 1986). Peripheral neuropathy secondary to DM is known to disrupt both the afferent and the efferent pathways causing postural instability (Uccioli et al. 1995). Moreover, limited joint mobility and reduced muscle strength are also associated with diabetic peripheral neuropathy (Rozadilla et al. 1991, Andersen, Gjerstad & Jakobsen 2004). Despite the evident influence of DMPN on postural stability, joint mobility and muscle strength there have been no attempts to evaluate the functional outcome in this patient group with the exception of one most recent study.

Ambrogi et al. (2005) interpreted the function of the foot in biomechanical terms as the ability of the foot to distribute the load and propel based on the mechanical properties of the plantar fascia and the Achilles tendon (Windlass mechanism) in diabetic patients (D'Ambrogi et al. 2005). They aimed to examine foot function in a case-controlled study wherein 61 patients with diabetes were compared with 21 healthy volunteers based on the Windlass mechanism (the synergic work of the Achilles tendon, plantar fascia and metatarso-phalangeal joints that locks the midtarsal bones and stabilizes the arch during propulsion) during the gait cycle. They concluded that the increased thickness of Achilles tendon and plantar fascia, which is more evident in the presence of neuropathy, may contribute to the overall increase of tensile force and to the occurrence of an early Windlass mechanism that is maintained throughout the whole gait cycle. The altered onset of Windlass mechanism was interpreted as abnormal foot function in diabetic patients by these researchers as it made the foot rigid and incapable of adapting to the ground resulting in high plantar pressures over the forefoot and heel that increase the risk of ulceration. The analytical approach adopted by this case-controlled study provides an insight into the pathomechanics of the ankle-foot complex due to diabetic foot complications during gait and its implications on plantar pressures. However, it fails to inform on any other aspects of foot function apart from gait.

In addition to this one report that described foot function in patients with DMPN, other studies describing the H-RQOL in diabetic patients were located (Anon 1996, Bott et al. 1998, Wandell & Tovi 2000, Manuel & Schultz 2004, Paschalides et al. 2004). Elderly diabetic patients have a poorer H-RQOL than the general population, especially in terms of physical health (Wandell & Tovi 2000). Anxiety, depression and negative beliefs about illness are known to influence the physical and mental functioning of these patients (Paschalides, Wearden, Dunkerley, Bundy, Davies & Dickens 2004). These studies report the H-RQOL in the general diabetic population but despite the negative effects of DMPN on posture and movement and the increased risk of further foot complications following DMPN, the specific impact of diabetic neuropathy on the H-RQOL remains unexplored. Evidence from published literature indicates that foot function and H-RQOL of the diabetic population begins to gain importance/attention only with further development of foot complications following DMPN namely foot ulceration, minor foot amputations and major lower extremity amputations (Price & Harding 1994, Garbalosa, Cavanagh, Wu, Ulbrecht, Becker, Alexander & Campbell 1996, Nehler et al. 2003).

2.4: Functional outcome in the presence of plantar ulceration:

Eighty-five percent of lower extremity amputations are preceded by foot ulceration (Reiber, Pecoraro & Koepsell 1992). Moreover, there is substantial morbidity, mortality and huge care costs in subjects with foot ulcers compared to those without ulceration (Ramsey et al. 1999, Tennvall & Apelqvist 2001). Despite the serious implications caused by diabetic foot ulceration (DFU), there is very little known about the functional outcome in people with diabetic foot ulcers other than the H-RQOL in this patient group.

Various generic H-RQOL questionnaires have been used to investigate the quality of life in this diabetic patient group in terms of physical (especially mobility), social and psychological impairments (Carrington et al. 1996, Tennvall & Apelqvist 2000, Meijer et al. 2001). H-RQOL of patients with current foot ulceration has been reported either in comparison with diabetic control subjects or in comparison with diabetic amputee patients or based on the reports from the group findings of DFU patients. It has been confirmed that the presence or history of DFU has a large impact on physical role, physical functioning and mobility. It was further believed that physical impairments influenced the QOL (quality of life) in these patients (Meijer, Trip, Jaegers, Links, Smits, Groothoff & Eisma 2001). Findings from two qualitative studies have reinforced the negative impact of DFU on the H-RQOL of these patients (Brod 1998, Ashford, McGee & Kinmond 2000). Vileikyte (2001) has documented that the loss of mobility associated with foot ulcers affects the patients' ability to perform simple, everyday tasks and to participate in leisure activities often leading to depression and poor QOL (Vileikyte 2001).

It therefore needs to be noted that the status of physical impairment and mobility of the diabetic patients with foot ulcers are based on self-reported measures from the diabetic patients and clinical judgements of the researchers. However, there is no objective documentary evidence based on performance-based measures to describe the physical impairments of this patient group.

Reports on comparison of patients with DFU to those with amputations and diabetic control subjects indicate that patients with DFU have poorer H-RQOL compared to the controls and those with minor LEA. However, diabetic patients with minor amputations have better H-RQOL than those with major LEA (Eckman et al. 1995, Carrington, Mawdsley, Morley, Kincey & Boulton 1996, Tennvall & Apelqvist 2000, Meijer, Trip, Jaegers, Links, Smits, Groothoff & Eisma 2000).

Eckman et al. (1995) reported that patients with DFU and those who had amputations rated their quality of life significantly poorer for physical functioning compared to diabetic controls. It was interesting to note that among the patients with amputations, the level of LEA determined physical functioning. Patients with foot ulceration had poorer scores than those with toe, trans-metatarsal and below-knee amputations but had better scores than those patients with above-knee amputations (Eckman, Greenfield, Mackey, Wong, Kaplan, Sullivan, Dukes & Pauker 1995).

Another study reported a similar pattern demonstrating that patients with ongoing ulcers have poorer HRQOL than patients with minor amputations. However, patients with major amputations are reported to demonstrate lower H-RQOL compared to patients with minor amputations (Tennvall & Apelqvist 2000). Carrington et al. studied the psychological status of the diabetic patients and reported that mobile amputees are known to present with better psychological status when compared to subjects with diabetic foot ulcer but not as good as diabetic controls (Carrington, Mawdsley, Morley, Kincey & Boulton 1996).

The evidence based on quantitative (case-controlled studies) and qualitative (semi-structured interviews) research studies primarily designed to evaluate H-RQOL in this patient group provides a detailed picture of various domains of H-RQOL of patients with diabetic foot ulcers. It is therefore clear that there is substantial literature to give an understanding of the H-RQOL of these patients but the remaining aspects of functional outcome need to be explored.

2.5: Functional outcome following partial foot amputation:

Currently, minor amputations and bypass graft surgeries are replacing below knee (BK) amputations in an attempt to impart better function to the residual lower limb (Van Damme et al. 2001). Despite the high risk of skin breakdown or higher amputation following trans-metatarsal amputations among subjects with DM (Mueller, Allen & Sinacore 1995) there is little empirical evidence addressing the issue of functional outcome following such procedures and its implications for Physiotherapy.

Hosch et al. (1997) reviewed the outcome of trans-metatarsal amputations (TMA) in patients with diabetes mellitus. The purpose of this study was to report the long-term outcomes of trans-metatarsal amputations secondary to sequelae of diabetes mellitus. A retrospective study was designed based on the data abstracted from 35 diabetic patients undergoing a TMA over a 6-month period in the year 1992. The patients were followed up for a mean 15.1±10.1 months and success of the amputation was defined as a process in which the patient retains his or her foot with complete re-epithelialization of the wound and ambulation without the use of prosthesis. Although this descriptive study was not designed primarily to evaluate the foot function following amputation, the definition of the success of the foot amputation reflects that the outcome of foot amputation is considered merely in terms of wound healing and the ability to walk without prosthesis. It lacked any consideration for instance, how they walk, how stable they are in terms of walking and what is the energy expenditure during walking.

Even before Hosch et al. (1997) reported their findings in terms of outcome following TMA, Garbalosa et al. (1996) had studied 10 diabetic patients with TMA with the objective of investigating foot function in terms of plantar pressures and kinematics of the ankle and foot motion. Peak plantar pressures in addition to static and dynamic range of motion of the ankle joint were assessed to grade the outcome of the surgery. Significantly greater mean peak plantar pressures were observed in the feet with TMA than in the intact feet of the same patients. A significantly greater maximum dynamic dorsiflexion range of motion was seen in the intact compared with the TMA feet (Garbalosa, Cavanagh, Wu, Ulbrecht, Becker, Alexander & Campbell 1996). This analytical study can be regarded as one of the early reports describing the kinematics of ankle-foot complex and plantar pressures of the affected and the contra-lateral foot in diabetic patients with TMA. However, it would be difficult to draw a complete picture of functional outcome of these patients based on the kinematics and plantar pressure distribution only. Moreover, it would be hard to grade their level of function without comparing these diabetic patients with TMA with their able-bodied counterparts.

Armstrong and Lavery (1998) reported similar findings when they compared the plantar pressures of subjects with partial foot amputations (n=27, isolated digit or ray amputations distal to the tarso-metatarsal joint) with diagnosed cases of DM (n=150) without history of plantar ulceration (Armstrong & Lavery 1998). They attributed the elevated plantar pressures to the higher prevalence of deformity and limited joint mobility following partial foot amputations. This report was based on a case-controlled study designed to examine the plantar pressure distribution of diabetic patients with partial foot amputations and therefore cannot be expected to inform the remaining domains of foot function in this patient group.

Later Mueller et al. (1997) reported on a fairly comprehensive approach to evaluate function in patients with TMA which was based on the findings from both self-reported and performance-based tests. They compared the function of patients with diabetes mellitus (n=15) and TMA (n=15) with that of age and gender-matched control subjects (Mueller, Salsich & Strube 1997). Function was measured using the Functional Reach Test (FRT), the Physical Performance Test (PPT), walking speed for 15.2 m (50 ft) and the Sickness Impact Profile (SIP). The PPT was administered as described by Reuben and Siu (1990) and included writing a sentence, simulated eating, lifting a book to put on a shelf, putting on and removing a jacket, picking up a penny from the floor, turning 360 degree, walking 16.4 m and climbing a single flight of stairs. The authors concluded that the subjects with TMA showed substantial functional limitations while wearing standard shoes with a toe-filler compared to age and gender matched controls. They attributed the limited function of these patients to their decreased foot length and loss of toes. Due to the shortened foot and loss of toes the subjects had difficulty in reaching, picking up a penny from the floor, walking at normal speed and stair climbing. This appears to be the only case-controlled study that has considered both constructs in the evaluation of function in this patient population i.e. performance tests and self-reported measures with the objective of informing a comprehensive picture of functional outcome. However, it lacks the conceptual framework underlying the approach of evaluation of functional outcome.

2.6: Functional outcome following trans-tibial Amputation:

Literature provides substantial evidence of the incidence of diabetic amputations, causal pathways of diabetic amputations, its impact on the quality of life and health care costs and mortality rate following diabetic LEA (Alpizar et al. 1995, Larsson &

Apelqvist 1995, Childs et al. 1998, Reiber et al. 1999, Tentolouris et al. 2004). It has also been observed that there has been extensive research on prevention and reduction of the incidence of LEA in the diabetic population (Apelqvist & Larsson 2000, Holstein et al. 2001, Tennvall & Apelqvist 2001, Meltzer et al. 2002, Driver, Madsen, & Goodman 2005). However, despite the serious implications of lower extremity amputations on the morbidity and mortality of the diabetic patients and the huge costs for the individual patient and the society, research on functional outcome in this patient group has been sparse.

Frykberg et al. (1998) investigated the outcome of lower extremity amputations in 41 patients (diabetic: n=27, non-diabetic: n=14) aged 80 years or older in terms of function, residential status and survival (Frykberg et al. 1997). The majority (66%) of the sample patient population had diabetes mellitus. Telephone interviews with patients or next of kin for patients who were deceased were undertaken for information regarding survival, functional and residential status. A simple survey instrument was used in which pre and post operative residential and functional status were assigned scores from 1-4 which were as follows: 1) living alone and independent, 2) living with family and ambulation with cane/walker, 3) Rehabilitation facility and in a wheelchair and 4) living in a nursing home and bed bound.

The results demonstrated that major lower limb amputation in the very elderly is associated with significant mortality and deterioration in function and living status. Fifty-five percent of elderly patients worsened in their ability to function independently after operation without respect for DM status. Although this study portrayed the significant deleterious effects of major LEA on longevity and lifestyle in the elderly patient there were several limitations. Relatively small sample size demands larger prospective studies. The authors have accepted that the functional and residential status scores were an arbitrary attempt to quantify these parameters of the quality of daily living of the patients. The scoring system may intuitively reflect the author's observations but it needs to be validated as a reliable instrument for assessing functional outcomes in such patients. Moreover, such a self-reported measure informs the patient's perception of function but has limitations in its ability to measure actual performance of the individual. Additionally although the observations are largely based on the diabetic patients who formed a major (66%) proportion of the study sample, the findings from the remaining 34% of non-diabetic amputee patients might have influenced the results. Furthermore these interpretations are restricted to elderly patients over 80 years and therefore do not represent the wide adult age group.

Another study reported the functional status of people with diabetes related lower extremity amputations based on Sickness Impact Profile (SIP). Thirty-five patients with DM with LEA were compared to 89 diabetic patients without amputation. The results demonstrated that both the physical dimension scores and the total SIP scores were significantly higher for amputee patients, higher scores indicating severe disability (Peters et al. 2001). However, the psychosocial dimension functional scores did not vary between the diabetic patients with or without an amputation. The authors also reported that there was no significant difference in the physical and psychological functional status between patients with higher levels of amputation (i.e. transtibial and transfemoral amputations) and patients with low levels of amputation (i.e. toe, transmetatarsal, Lisfranc and Charcot amputations). This is a commendable report based on a robust case-controlled study, which provides an elaborate description of the H-RQOL of diabetic patients with LEA. However, the limitation of such an approach to investigation of functional status lies in the fact that it is purely based on a self-reported measure and therefore misses the construct of functional evaluation based on performance tests.

Another study reported the H-RQOL in 60 randomly selected patients with dysvascular trans-tibial amputations (causes included diabetic foot complications and peripheral vascular disease) the majority of which were diabetic (n=44: DM i.e. 73%). A linear analog format of the Prosthetic Evaluation Questionnaire was used to measure H-RQOL in terms of prosthesis function, mobility, psychological response, well-being and satisfaction. All the patients scored the best in the psychological domain and lowest in the mobility domain warranting a purposefully designed rehabilitation program for these patients to optimise their level of function (Harness & Pinzur 2001). As commented earlier there is a possibility that the findings of this descriptive study were influenced by the 27% of non-diabetic dysvascular patients with TTA although the interpretations were largely based on the 73% diabetic patient group.

Recently Nehler et al. (2003) evaluated functional natural history of patients undergoing major lower extremity amputations based on a retrospective review. One hundred and fifty-four patients with 172 major amputations (78 Above-knee i.e. AKA and 94 below-knee i.e. BKA) because of either critical limb ischemia (87%) or DMPN (13%) were followed up for a mean period of 14 months. Function was assessed in surviving patients at 10 and 17 months respectively and reported in terms of the degree of ambulation, (e.g., outdoors, indoors only, or no ambulation) use of a prosthesis and independence (e.g., community housing or nursing facility). Based on their findings at 10 and 17 months respectively, 21% and 29% of patients ambulated outdoors, 28% and 25% ambulated indoors only, and 51% and 46% of patients were non-ambulatory. Thirty-two percent and 42% of patients used prosthetic limbs and 17% and 8% of patients who lived in the community before amputation required care in a nursing facility (Nehler, Coll, Hiatt, Regensteiner, Schnickel, Klenke, Strecker, Anderson, Jones, Whitehill, Moskowitz & Kurpski 2003). Although this study reports finding from an extensive review based on a substantial number of patients undergoing major LEA and provides crucial information regarding their ambulatory status it is noted that ambulation alone is equated to functional outcome. Moreover, the terms such as 'functional outcome' and 'quality of life' are used interchangeably without any conceptual rationale.

Most recently, Levin (2004) reported a review of literature to discuss the functional outcome following major LEA as it relates to the geriatric population (Levin 2004). The author defined functional outcome as an individual's ability to perform activities after LEA and concluded that there is a significant difference in function among older individuals who have had LEA. Based on the review of literature it was inferred that the functional tests are limited in their ability to predict functional outcome in this population. Many functional tests examine only physical function, while others study cognitive or social function. The author identified that it is the combination of these functions that will determine the overall performance of an individual after LEA.

Even the observations from the present literature review indicate that the tests designed to evaluate the functional outcome of diabetic patients with LEA are limited in their ability to test the different domains of functional outcome. The terms 'functional status' and 'H-RQOL' are used interchangeably and the reports are largely based on the findings from H-RQOL measures as H-RQOL measures appear to be popular outcome measures for investigation of functional outcome.

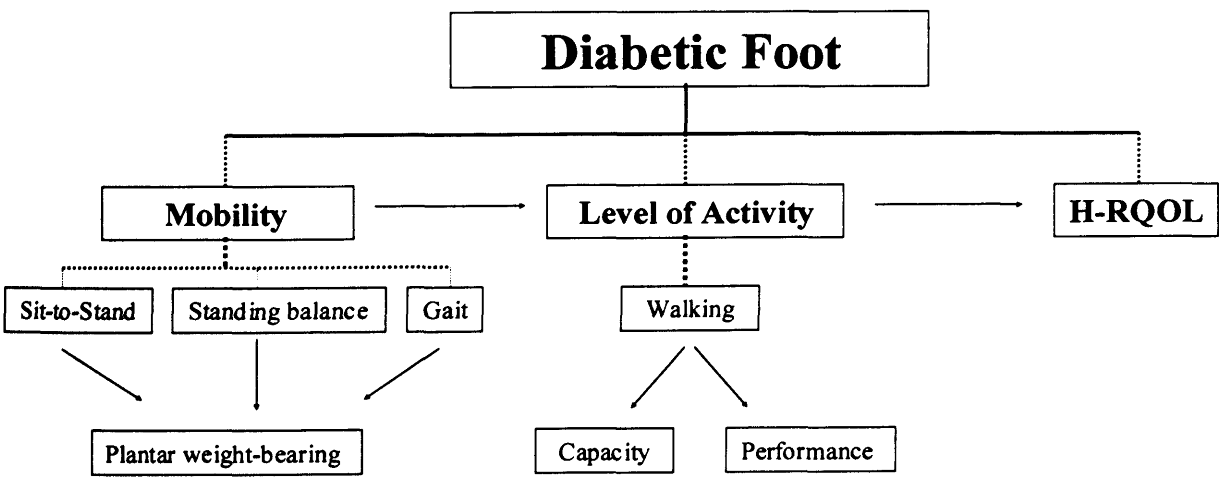
To summarise, the review of literature indicates sparse and diverse attempts to evaluate the functional outcome in diabetic people with foot complications. There is an evident lack of conceptual clarity in the overall interpretation of function. Although all these studies provide crucial information pertaining to the singular aspect of physical function, social function and psychological status of these patients there is lack of evidence to indicate the overall performance of these patients in different dimensions of functional outcome. However, H-RQOL appears to be a popular outcome measure in diabetic patients with plantar ulceration and LEA. All these observations warrant a need for a comprehensive model to evaluate functional outcome in these patients.

2.7: Proposed model to evaluate functional outcome:

The increased physiological and psychological stress imposed on the body by the changes occurring in the diabetic foot needs to be investigated at a greater depth in wider dimensions of functional outcome rather than continuing with the conventional univariate approach of measuring only the joint mobility or muscle strength or plantar pressure distribution in such people. As stated by Hurley (2001) it is far more important to measure the correct thing imperfectly than to measure precisely, that which is merely convenient or standard. The existing diverse array of definitions of foot function reflects the need for organising the various outcome measures to construct a unified, comprehensive and robust model to evaluate function. Findings from a comprehensive functional evaluation can have valuable implications for prophylactic care, early identification of potential risk factors and holistic rehabilitation.

Therefore, it was proposed to investigate the various components of the physical domain and the domain of H-RQOL of functional outcome, namely the essential tasks of mobility and its impact on weight-bearing, level of activity and H-RQOL. Although diabetes presents with limited joint mobility in the hands as a form of clinical manifestation of musculo-skeletal involvement in the upper limbs (Guyton & Saltzman 2001), diabetic foot disease will have a direct impact on lower extremity related function. Therefore, the proposed model focuses on domains related to lower extremity function (Figure 2.1).

Figure 2.1: Proposed model of functional outcome



The foot is an engineering marvel that allows the body to perform many physical activities over a wide variety of terrain with remarkable efficiency. However, the concept of foot function is complex because the functions of the foot and the lower extremities are biomechanically integrated. Effectively normal foot function requires normal lower-extremity function and vice versa (Kirby 2000). Moreover, to evaluate the overall performance of an individual in his or her own environment in the presence of diabetic foot complications, functional assessment needs to extend beyond the biomechanical analysis of gait in the laboratory. Therefore the proposed model is designed to assess the functional outcome based on essential components of the physical dimension of function (mobility tasks and level of activity and their impact on the weight-bearing ability of the feet) related to the lower extremities and H-RQOL in the presence of diabetic foot complications.

The present study attempts to evaluate foot function with a model, which shadows the ICF model of function (ICF 2002). However, the ICF model cannot be applied in its present total form to address the research question of this study. ICF is primarily designed to find a role in the planning and implementation of health care services (ICF 2002) and therefore when the concept of function is applied to the research sector it needs to be approached with a combination of clinical relevance and scientific investigation. The ability to perform the fundamental tasks of mobility, which are essential components of ADL, is central to the proposed model of function because successful performance of these tasks can be considered as the keystone of functional independence. Kinesiological analysis can inform a complete examination of the physical aspect of a movement or an activity.

Therefore, the approach to the analysis of function in the present study is predominantly kinesiological. Kinesiology is defined as the science of movement comprising two major components: Kinetics and Kinematics. Kinetics involves the study of forces governing the movement and Kinematics deals with the study of motion irrespective of the forces, which govern the movement. However, this model does not restrict itself to strict biomechanical analysis, but is constructed to understand biomechanics with an underlying objective of clinical application. Therefore although the model has a perspective of clinical kinesiology, it is not designed to delve deeper into the biomechanics of each movement, but analyse the alterations in movement in the presence of diabetic foot complications and the implications of the same to clinical practice. Appropriate reliable and valid outcome measures were identified to construct each domain of function, which are presented below.

2.7A: Impairment:

A problem in body function or structure such as a significant deviation or loss is interpreted as impairment (ICF 2002). The primary impairment common to all the patients in the present study was diabetic peripheral neuropathy (DMPN).

Diabetic foot disease is a multi-factorial disorder. In addition to the heterogeneous nature (sensation, motor control, pain, proprioception and autonomic functions) of diabetic neuropathy producing a variable course of the diabetic foot disease, limited joint mobility is also known to co-exist. However, somatic neuropathy is the most widely recognised pattern presenting with diminished distal sensation as its hallmark (Guyton & Saltzman 2001). Loss of sensation due to peripheral neuropathy is central in the aetiology of ulceration (Pecoraro, Reiber & Burgess 1990). Some authors have reported that DMPN shows a progressive trend with limb amputation as the final end-point of the disease (Sima & Greene 1995). Therefore accurate assessment of the sensory component of DMPN gains prime importance in the provision of prophylactic care in diabetic patients. Consequently, the value of screening patients with peripheral neuropathy is gaining rapid recognition in diabetic foot care (Holewski et al. 1988, Kumar et al. 1991, Perkins et al. 2001, Nwabudike, Coravu & Ionescu-Tirgoviste 2004).

Several methods have been documented in the literature to detect diabetic peripheral neuropathy such as assessment of touch-pressure sensation, vibration perception threshold and electro diagnostic studies (Halar et al. 1982, Dyck et al. 1983, Bloom et al. 1984, Lowenthal & Hockaday 1987, Dyck 1988, Maser et al. 1989, Masson et al. 1989, Armstrong et al. 1991, Kumar, Fernando, Veves, Knowles, Young & Boulton 1991, Young, Every, & Boulton 1993, Bril 1994, Chaudhry et al. 1994, Mueller 1996, Simoneau et al. 1996, Cavanagh, Ulbrecht & Caputo 1996, van Deursen et al. 2001, Anon 2004). It is agreed that both quantitative sensory testing and electro-physiological tests can detect and quantify peripheral neuropathy (Report and recommendations of the San Antonio conference on diabetic neuropathy 1987). Despite their simplicity, quantitative sensory tests appear to be better at defining loss of protective sensation than electro-physiological tests (Birke & Sims 1986, Holewski, Stess, Graf & Grunfeld 1988, Cavanagh, Simoneau & Ulbrecht 1993). Quantitative sensory testing includes both pressure and vibration perception and they both have been shown to be strongly associated with foot ulceration (Boulton et al.

1986, Sosenko et al. 1990). However, vibration perception threshold (VPT) may vary widely between tests and sites for the same patient (Williams, Gill & Aber 1988). Therefore, the Semmes-Weinstein monofilaments (S-W monofilaments) have been chosen to be the best reliable measure of loss of protective sensation (Birke & Sims 1986, Holewski, Stess, Graf & Grunfeld 1988, Kumar, Fernando, Veves, Knowles, Young & Boulton 1991, Cavanagh, Simoneau & Ulbrecht 1993, Mueller 1996). It is the modified form of Von Frey hair instrument, which has been used for decades to test touch perception threshold (Halar, Hammond & LaCava 1987). The 5.07 monofilament is known as the best indicator of protective sensation and risk determinator for foot ulceration (Birke & Sims 1986, Holewski, Stess, Graf & Grunfeld 1988). Therefore, the 5.07 S-W monofilament was chosen to confirm the loss of protective sensation as an indicator of DMPN in the present study. It has been confirmed that the inability to feel the 5.07 S-W monofilament represents a sensory threshold that is more than 50 times compared to normal, implying that roughly 98% of the sensory ability has been lost (Jeng, Michelson & Mizel 2000). Moreover, the aim of the study was not to monitor the progression of DMPN over time and therefore S-W monofilament is proposed against quantification of vibration perception threshold or electrodiagnostic studies (Asbury & Porte 1988). Presence or absence of vibration sensation using a tuning fork is proposed only to corroborate the findings from S-W filament testing.

Current clinical practice reflects that conventionally, most clinical settings would limit the assessment of the diabetic foot to this stage. However considering the impact of DMPN on postural stability, gait and plantar pressure distribution (Simoneau et al. 1994, Frykberg, Harvey, Lavery, Harkless, Pham & Veves 1998, Dingwell et al.

2000) the proposed model extends further to explore the impact of this impairment on various domains of functional outcome beginning with the domain of mobility.

2.7B: Mobility:

The concept of physical mobility can be interpreted in several dimensions. WHO defines mobility as 'the individual's ability to move about effectively in his surroundings' (WHO, 1980). This definition of mobility can be criticised to inform only the aspect of ambulant mobility. In a more general and comprehensive sense mobility can be defined as the process of moving oneself and of changing and maintaining postures (Bennekom van, Jelles & Lankhorst 1995). The proposed model of function will use the general concept of physical mobility because such a comprehensive interpretation of mobility is necessary to identify specific problems encountered during the fundamental tasks of mobility and plan an appropriate rehabilitation programme for the diabetic neuropathic patients at various stages of foot complications.

Furthermore, the present model is designed to measure mobility from both perspectives: 'professional' (wherein the mobility of the subject is assessed by an objective expert or objective instrument, independent of personal feelings or prejudices) and 'patient' (wherein the subject's mobility is assessed by the subject himself) (Buford 1995, Hobart, Freeman & Lamping 1996, Bussmann & Stam 1998). Therefore, it is proposed that mobility will be assessed based on performance measures and self-reported measures for a complete evaluation of what the subjects actually do in everyday life and what they think they do. The fundamental tasks namely STS, standing & gait are proposed to assess the domain of mobility with the objective of identifying the problem areas while performing these tasks and guiding clinical decisions regarding the independence and safety of the patients. STS is considered as the keystone of ambulant mobility and is an important functional skill (Cahill, Carr & Adams 1999). Therefore, assessment of mobility is proposed to begin with analysis of the sit-to-stand movement followed by balance in quiet standing and analysis of walking activity. Plantar pressure distribution during walking is proposed as a measure of plantar weight bearing. Rivermead Mobility Index is proposed as a self-reported measure of mobility (Collen et al. 1991) to include the patients own perception of all these tasks of mobility.

Performance-based measures:

Sit-to-stand:

Transfer to a standing posture from sitting is an important functional task (Vanderlinden, Brunt & McCulloch 1994). It is critical to independent living since it is necessary in order to stand and to walk (Khemlani, Carr & Crosbie 1999). Due to the inability to raise from a chair many potentially, ambulant patients and elderly people remain prisoners in their chairs (Kerr et al. 1991). However, it is one of the most mechanically demanding functional tasks among daily activities (Riley et al. 1991). The hip and the knee are subjected to higher forces in rising from sitting compared to activities such as gait, stair ascent and other exercises (Hodge, Fijan & Carlson 1986, Berger et al. 1988). Yet it is a commonly performed ADL and is a cornerstone of ambulant mobility. Therefore, it could be considered as the first milestone (crucial activity) in the investigation of mobility of this patient population at different stages of diabetic foot complications.

The importance of this fundamental task of mobility is widely recognised in elderly people (Alexander et al. 1997, Papa & Cappozzo 2000, Schlicht, Camaione & Owen 2001, McCarthy et al. 2003) and patients with various neurological, orthopaedic and other health related conditions such as paraplegia, hemiplegia, knee arthroplasty, obesity, Parkinson's disease, cerebral palsy, chronic low back pain, rheumatoid arthritis and traumatic brain injury (Berger, Riley, Mann & Hodge 1988, Gioftsos & Grieve 1996, Munro et al. 1998, Bahrami et al. 2000, Galli et al. 2000, Brunt et al. 2002, Zablotny, Nawoczenski & Yu 2003, Cheng et al. 2004, Hennington et al. 2004, Inkster & Eng 2004). Extensive attempts have been made to study the mechanics of this task and identify the determinants affecting the performance of movement with the objective of providing maximal functional independence, safety and efficiency of movement in these people. However, despite the impact of diabetic foot disease on lower extremity range of motion and muscle strength, no evidence was located to understand the mechanics of STS task in this patient group.

Quiet standing:

Balance and function are inextricably linked. Balance is not an isolated quality but underlies our capacity to undertake a wide range of activities that constitute normal daily life (Huxham FE 2001). Balance forms the foundation for all voluntary motor skills (Massion & Woollacott 1996). Therefore, assessment of balance in the standing position is necessary to ensure the safety of the individual in that position.

Moreover, standing is one of the most common postures essential for activities of daily living. It is the kinesiological link between sit-to-stand transfer and walking and therefore could be considered as the second milestone of ambulant mobility, which needs investigation. It becomes even more vital to assess standing balance in patients with DMPN considering the postural instability caused by peripheral neuropathy (Uccioli et al. 1995). Several studies have confirmed the impaired balance in standing posture resulting in patients with diabetic peripheral neuropathy (Cavanagh, Simoneau, & Ulbrecht 1993, Uccioli et al. 1995, Giacomini et al. 1996, Katoulis et al. 1997).

However, balance control in the presence of foot ulceration, partial foot amputations and trans-tibial amputations in diabetic patients has not received much attention. Only one case-controlled study has reported increased postural instability in patients with prior ulceration compared to those without history of foot ulcers (Katoulis et al. 1997). This study can be considered as the only report presenting findings from diabetic patients with history of ulceration without attempts to investigate the balance of patients in the presence of ulceration. Lack of evidence related to balance control in patients with active ulceration suggests that it is probably only assumed that balance is impaired in these patients without any empirical evidence to confirm its severity.

Although balance has not been studied specifically in diabetic amputee patients, patients with diabetes related amputations have formed the broad group of dysvascular amputee patients whose balance has been compared to patients with trauma related amputations (Hermodsson et al. 1994, Nadollek, Brauer & Isles 2002). Amputee patients are known to demonstrate impaired standing balance compared to the healthy subjects regardless of the cause of amputation (trauma or vascular disease) (Fernie, Eng & Holliday 1978, Isakov et al. 1992, Hermodsson, Ekdahl, Persson & Roxendal 1994). Impaired sensory feedback due to DMPN is speculated to worsen the standing balance in diabetic neuropathic patients with partial foot amputations or trans-tibial amputations thereby necessitating the need for further investigation.

Quiet stance has been used to assess the human postural control during upright stance (Hsiao-Wecksler et al. 2003). In the present study, it is proposed to assess quiet standing using static posturography wherein the motion of the COP is measured as the subject quietly stands on a force platform (Panzer, Bandinelli & Hallett 1995). The COP is the point of application of the resultant of the vertical ground reaction forces (Viton et al. 2000) which was determined from the force platform in the present study.

Gait:

Walking is the ultimate goal of ambulant mobility representing an integral activity of daily life. It serves as an individual's basic need to move from one place to another (Simoneau 2002). Walking is a complex task, which requires the CNS to generate appropriate motor actions from the integration of visual, proprioceptive and vestibular sensory inputs (Simoneau 2002). Therefore, impaired sensory feedback due to DMPN is known to cause alterations in gait pattern (Courtemanche et al. 1996, Menz, Lord, St George & Fitzpatrick 2004). These alterations are likely to be pronounced with the further development of diabetic foot complications namely plantar ulceration, partial foot amputations and trans-tibial amputations.

A review of literature clearly demonstrates a wide gap in the literature indicating that the gait of patients with current plantar ulceration has not received much attention. Probably the dilemma between allowing weight-bearing or non weight-bearing during the phase of active ulceration may have discouraged researchers from exploring this area. However it needs to be understood that although the dilemma regarding weight-bearing ('yes or no' and 'if yes, how much') in the presence of plantar ulceration is not resolved, patients with DFU continue to ambulate for daily function. Therefore, it can be argued that analysis of gait is essential as it is crucial to inform clinical practice regarding the modifications in gait and cautions to be exercised.

Studies describing gait alterations following partial foot amputations in diabetic patients (Hosch, Quiroga, Bosma, Peters, Armstrong & Lavery 1997, Mueller, Salsich & Strube 1997) and trans-tibial amputations (Winter & Sienko 1988) already exist. These studies have evaluated gait alterations produced by patients following lower extremity amputations and identified the compensatory strategies adopted to walk. There are also several other studies which have investigated the energy cost of gait following trans-tibial amputations (Colborne et al. 1992, Casillas et al. 1995, Waters & Mulroy 1999). Yet other studies have reported the effect of various prostheses on gait following TTA (Hannah, Morrison & Chapman 1984, Colborne, Naumann, Longmuir & Berbrayer 1992, Powers et al. 1994, Snyder et al. 1995, Lehmann et al. 1998). However in most studies evaluating gait following TTA, diabetic amputee patients are included either as part of the general amputee group or as part of the dysvascular amputee group. Some studies report their findings from a general group of amputee patients irrespective of the cause of amputation whereas others classify them broadly as traumatic and dysvascular amputee groups. Such an observation may emerge probably because the literature has not demonstrated sufficient evidence to treat the diabetic neuropathic amputee group as an exclusive patient group during investigation and rehabilitation. Moreover, there is currently no evidence to illuminate gait performance across the four diabetic neuropathic patient groups at consequent stages of foot complications namely DMPN, DFU, PFA and TTA.

Therefore, it is proposed to investigate the spatial and temporal parameters of gait in addition to gait kinetics. The impact of weight-bearing on insensate feet during walking will be studied in terms of plantar pressure distribution. All these gait parameters will provide a complete kinesiological analysis of the gait cycle.

Self-reported measure:

It has been established that performance-based measures of functional status are modestly associated with self-reported measures on a cross-sectional as well as longitudinal basis. The 2 measures of functional status appear to be complementary rather than being two measures of the same concept (Hoeymans et al. 1996). Therefore, to provide a complete account of the functional outcome of patients with diabetic foot complications it was proposed to account for the patients their own perception in addition to the assessment of their actual performance.

Rivermead Mobility Index:

One of the most important health care developments made is an increasing consensus regarding the centrality of the patient's point of view in monitoring medical care outcomes (Geigle & Jones 1990). Such a perspective makes the individual's own perception of mobility as crucial as performance-based measures in the assessment of mobility. Rivermead Mobility Index suits the purpose well since it is a short, simple and clinically relevant tool, which concentrates on body mobility (Collen et al. 1991). It has a hierarchy of 15 mobility items from turning in bed to running. Therefore it seems the most appropriate tool to express the patient's own perception of mobility which includes all the three mobility items (STS, standing balance and walking) assessed with performance based measures.

Literature has discussed the role of RMI in the assessment of mobility in patients with LEA, stroke, multiple sclerosis and elderly people (Vaney et al. 1996, Wright, Cross & Lamb 1998, Lennon & Johnson 2000, Franchignoni et al. 2003). When RMI was applied in lower limb amputees, it emerged as an ordinal measure with adequate levels of a series of psychometric properties. However, no attempts have been made to investigate the mobility of diabetic neuropathic patients with RMI. Additionally there is no evidence to indicate the patient's perception of mobility at consequent stages of diabetic foot complications.

Plantar pressure distribution:

Diabetic foot complications are known to alter the plantar pressure distribution predisposing the foot to potential risk of ulceration (Veves, Vanross & Boulton 1992, Katoulis, Boulton & Raptis 1996, Armstrong & Lavery 1998). Since all three mobility tasks (sit-to-stand, standing and walking) are weight-bearing in nature it is essential to study the impact of sit-to-stand, standing and walking on plantar weight-bearing in this patient population which is already at risk of ulceration from DMPN. Findings from the assessment of plantar pressures over the affected and the contra-lateral foot will provide a clear picture of the severity of risk involved in weight-bearing during walking in the presence of diabetic foot disease.

Plantar weight-bearing during sit-to-stand is the least understood. Although there is not much literature to discuss plantar pressures during standing, a few studies have documented the pressure distribution in standing.

The pressures during standing appear to be much lower compared to the pressures during walking (Gefen 2003, Burnfield et al. 2004). Rozema et al. (1996) also reported that compared with standing, most dynamic activities of daily living (slow and fast walking, slow running and turning) result in much higher plantar pressures in all anatomical foot regions. The only two activities that did not demonstrate higher pressures compared to standing were rising from and sitting down in a chair (Rozema et al. 1996). They found that the more active ADL e.g. fast walking, running resulted in higher pressures than in normal walking and the pressures were higher in some forefoot sites during turning and stair walking compared to normal walking. Considering the existing risk for plantar injury due to diabetic neuropathy (Katoulis, Boulton & Raptis 1996, Plank, Wilcox & Hyer 1999) it was not fair to test the participants during the more active activities. Therefore, the present study will focus on plantar pressure distribution during walking because it is established that the plantar pressures are higher only during the more vigorous activities than walking.

Moreover, it is known that walking is the most common daily task and the pressures during walking correlate highly with pressures during ramp climbing, turning and stair climbing in patients with DM and peripheral neuropathy (Maluf et al. 2004). Therefore, clinical evaluation of peak pressures during walking can be considered as an efficient method to screen the maximum levels of plantar stress as patients with DMPN perform their daily activities (Maluf et al. 2004).

It is already established that peak plantar pressures increase with DMPN (Katoulis, Boulton & Raptis 1996, Plank, Wilcox & Hyer 1999) and they demonstrate a further rise with plantar ulceration especially over the fore-foot where the ulcers occur commonly (Mueller 1995). Partial foot amputations are known to cause higher plantar pressures because of the decreased weight-bearing surface area (Armstrong & Lavery 1998). However, the plantar pressure distribution over the surviving foot following major lower extremity amputations has not received much attention until relatively recently (Veves, Vanross & Boulton 1992). Although it would appear logical to speculate that the contra-lateral foot may be at an increased risk of ulceration in the presence of unilateral plantar ulceration or foot amputation, evaluation of plantar loading over the surviving foot has not received any attention. Therefore, the instantaneous pressure pattern i.e. Maximum Peak Pressure (MPP) and Pressure-time Integral (PTI) over the affected and the contra-lateral foot is essential to compare the plantar loading in these patient groups.

In addition to the instantaneous pressure picture from the supervised walking in the laboratory environment, it would be interesting to evaluate the effect of daily cumulative stress on the plantar tissues. Moderate repetitive stress is known to cause ulceration (Bauman & Brand 1963, Bauman, Girling & Brand 1963) as much as high instantaneous pressure. There have been attempts to evaluate daily plantar cumulative stress (DPCS) in the diabetic neuropathic patients (Maluf & Mueller 2003). Daily Plantar Cumulative Stress is described as the product of PTI and average daily strides. They have reported that the tissue atrophy and weakness resulting from decreased DPCS and the sudden alteration in the DPCS due to sudden variations in walking activity contribute to plantar tissue injury (Maluf & Mueller 2003, Lott et al. 2005). However, there are no reports to compare the DPCS in diabetic neuropathic patients at consequent stages of foot complications.

Therefore the instantaneous pressure picture i.e. Maximum Peak Pressure (MPP) and Pressure-time Integral (PTI) along with the Daily Cumulative Plantar Stress (DCPS) over the affected and the contra-lateral foot is essential to provide a complete picture of plantar loading in these patient groups.

2.7C: Activity level:

Level of activity forms the intermediate domain in the proposed model of function. As per the International Classification of Function (ICF) activity is the component of function which involves execution of a task or action by an individual (WHO 2002). Walking is an important and most common activity of day-to-day function, which reflects the actual level of mobility of an individual in her or his own environment. Therefore analysis of walking would be the most appropriate to grade the level of activity. Although the limitation in activities related to the upper limbs due to the decreased joint mobility in the hands cannot be overlooked (Guyton & Saltzman 2001) it is believed that diabetic foot disease will have a direct impact on lower extremity related function. Therefore, the proposed model evaluates walking to grade the level of activity.

It can be argued that high impact activities such as running, jogging and sprinting are also activities related to the lower-extremity, which could be investigated. However, the proposed model stops at the evaluation of walking for two reasons. Patients with active foot ulceration cannot run. In the case of the remaining three groups (DMPN, PFA & TTA) it is not clear whether the diabetic patients with foot complications in the presence of symptomatic or non-symptomatic multi-system problems can accomplish such high intensity activities. Secondly, even if the general health status allowed such high impact activities, it is doubtful whether these patients should be allowed to perform such vigorous activities in the presence of risk factors such as diabetic neuropathy, which make the plantar tissues vulnerable to injury (Gefen 2003).

The domains of this component (activity) are qualified by the two constructs: capacity and performance (ICF 2002). The capacity qualifier describes an individual's ability to execute a task or an action. Therefore, Total Heart Beat Index (THBI) is proposed to measure the capacity of walking as an index of energy expenditure (Hood et al. 2002). The performance qualifier describes what an individual does in her or his current environment. Therefore, the performance of walking activity is proposed to be measured in terms of average daily strides using the Step Activity Monitor (Shepherd et al. 1999).

Capacity of walking activity:

It is proposed to assess the capacity of walking by measuring the energy expenditure during walking. Energy expenditure has traditionally been measured either by indirect calorimetry (VO_2 measurements) or by the Physiological Cost Index. VO_2 measurements however require equipment, which is cumbersome and may cause discomfort to the user, possibly affecting the results obtained. Whereas PCI requires that, the working heart rate must achieve a steady state. In unimpaired subjects, this state occurs when the cardiovascular system has adapted to the new physiological demands, which occurs approximately in the third minute of exercise (Hood, Granat, Maxwell & Hasler 2002). It may not be ethically sound to subject patients with plantar ulceration to prolonged periods of walking necessary to attain the steady state of exercise. Therefore Total Heart Beat Index is proposed to represent the energy efficiency of gait under non-steady-state conditions (Hood, Granat, Maxwell & Hasler 2002) since it is a valid and reliable tool (THBI had very high reproducibility for steady-state exercise, ICC=0.950 and high reproducibility under non-steady state conditions, ICC=0.893).

Energy expenditure during gait has been widely researched in a variety of disorders such as hip and ankle athrodesis, knee immobilization, spinal cord injury, hemiplegia and cerebral palsy. (Hash 1978, Waters et al. 1982, Waters & Lundsford 1985, Waters et al. 1988, Rose et al. 1990). The most popular patient group was the patients with LEA (Gonzalez, Corcoran & Reyes 1974, Pinzur et al. 1992, Jaegers et al. 1993, Hoffman et al. 1997). Within the amputee population, it has been established that higher levels of amputations correspond with greater levels of energy expenditure (Waters & Mulroy 1999). However, the trend in energy requirement of the diabetic patients with consequent stages of foot complications remains unexplored.

Performance of walking activity:

Average daily stride count is proposed to indicate the performance of walking. Measurement of daily walking as an outcome measure has gained popularity in the recent past (Bassey, Davies & Kirby 1983, Hutchinson et al. 1995, Yamanouchi et al. 1995, Armstrong & Boulton 2002, Hartsell et al. 2002, Atkinson, Goody & Walker 2005, Bates et al. 2005, Lott et al. 2005). Researchers have confirmed that the correlation between actual walking (performance-based measure) and self reported measure to grade the physical activity is not as strong (correlations between total daily steps and the SF-36 Physical component summary score, Physical function, Bodily pain and Vitality scales were r=0.376, 0.488, 0.332 & 0.380 respectively) as it was believed by some (Smith et al. 2004). Consequently, several studies have quantified daily walking activity in patients with neurological disorders (Busse, van Deursen & Wiles 2003, Busse et al. 2004, Pearson et al. 2004).

It has been evaluated in the diabetic population as well with the objective of providing sample comparisons (Tudor-Locke, Bell, Myers, Harris, Lauzon & Rodger 2002). Apart from providing the data for the diabetic population measurement of walking activity has been explored to closely monitor the risk of ulceration in these patients (Armstrong et al. 2001, Armstrong et al. 2004). It has been demonstrated that sudden variation in walking activity may lead to plantar tissue breakdown (Armstrong, Lavery, Holtz-Neiderer, Mohler, Wendell, Nixon & Boulton 2004, Lott D 2005). However, there are no reports to demonstrate the comparison of walking activity in the diabetic neuropathic patient groups at consequent stages of foot complications. Therefore, it is essential to quantify daily walking in these patient groups to grade their level of activity.

Although there is no clear standard of measurement of actual walking in the community setting, (Bussmann & Stam 1998) step activity monitors have been shown to be valid and reliable tools (overall, the step activity monitor had 2.28% less absolute error than the pedometer $p=0.005$ during a variety of ambulatory activities such as slow and brisk walking and ascending and descending stairs) of objective quantification of daily walking activity (Shepherd, Toloza, McClung & Schmalzried 1999). Step activity monitors do not provide any feedback to the subjects thereby allowing an unobtrusive measure of actual walking in their environment. Moreover, they are not biased by overweight or the presence of lower extremity joint prosthesis

(Shepherd, Toloza, McClung & Schmalzried 1999) and therefore suited the study population, which included a group of diabetic patients, which had unilateral TTA and was likely to be above normal BMI.

2.7D: H-R QOL:

Quality of life has now become firmly established as an important endpoint in medical care (Anon 1995). This is especially true of chronic diseases for which a cure is unlikely (Smith, Avis & Assmann 1999) and diabetes mellitus is a classical example of such a chronic disease. Quality of life (QOL) is defined as the physical, social and psychological functioning of the patients as being influenced by disease or therapy (WHO 1959, Revicki 1990, Fitzpatrick 1992). However, H-R QOL is more specific and more appropriate in the assessment of QOL in the presence of a specific health condition. It refers to the patient's appraisals of their current level of functioning and satisfaction compared to what they perceive to be ideal (Cella & Tulsky 1990). Therefore, evaluation of H-RQOL was proposed to provide comprehensive information regarding the functional outcome in people with diabetic foot complications. It is a multidimensional construct, which can be measured using a generic or condition specific tool.

It could be argued conceptually whether H-RQOL should be treated as a part of functional outcome or whether it should be considered as an autonomous construct. It is already recognised that 'perceived health status', 'functional status' and 'quality of life' are three concepts often used interchangeably to refer to similar domains of 'health' (Guyatt et al. 1996). Researchers have also identified that the boundaries of definition usually depend upon why one is assessing health and the particular concerns of patients, clinicians and researchers (Guyatt, Jaeschke, Feeny & Patrick 1996). In a similar context, it needs to be highlighted that the focus of the present study was to evaluate the functional outcome of patients with foot complications. Therefore, it is proposed to assess H-RQOL to complete the information related to function with the primary focus on functional health status.

SF-36 is proposed as a generic tool (Ware et al. 1993) and Cardiff Wound Impact Scale (CWIS) as a condition-specific tool (Price & Harding 2004) to investigate the H-R QOL. The choice of the two assessment tools was based on the objective of evaluating H-R QOL from different but complementary perspectives.

There are several generic and disease specific tools available for evaluation of H-RQOL e.g. Sickness Impact Profile (SIP), Disease specific quality of life scale (DSQOLS) and Diabetes quality of life questionnaire (DQLCTQ) (Bott et al. 1998, deGrauw et al.1999, Shen et al. 1999). However, they were not suitable for the present study either because the questionnaire were developed primarily to investigate the outcome of the different treatment regimens (DSQOLS & DQLCTQ) or the questionnaire was too extensive (SIP). Because the focus of the study is to evaluate functional outcome and SF-36 is primarily designed to investigate the functional health status, SF-36 appeared to be the most appropriate tool for assessment.

A generic measure is selected with the intention of comparing the study population (in this case the diabetic population) with the normal population within similar age groups (Price 2004). Whereas a condition specific-tool is used to investigate the impact of diabetic foot complications on the patient population studied (Price 2004).

SF-36 has already been used to investigate the H-RQOL in diabetic neuropathic patients, diabetic patients with active ulceration and diabetic patients with healed ulcers (Ahroni & Boyko 2000, Nabuurs-Franssen et al. 2005). The authors concluded that the appearance of any neuropathic complication was associated with a decline in H-RQOL. It was also demonstrated that diabetic patients with a healed foot ulcer have a higher H-RQOL than patients with a persisting ulcer. However, no published reports were located describing the investigation of H-RQOL in patients with PFA and TTA. In addition, no studies have so far compared the H-RQOL in patients with consequent stages of foot complications namely: DMPN, DFU, PFA and TTA. Moreover, there is no evidence to indicate the course of the H-RQOL in diabetic patients at consequent stages of foot complications using SF-36.

2.8: Features of the proposed model of function:

The proposed model is designed to evaluate functional outcome in the domains of impairment, mobility, activity and H-RQOL. Such a comprehensive model of function is in tune with the changing focus of WHO from merely 'life expectancy' to 'healthy life expectancy'. Life expectancy estimates determine the overall length of life based on mortality data, without considering quality of life as aging progresses, whereas the concept of 'healthy life expectancy' deals with the expected number of years a person might live in the equivalent of full health (McArdle, Katch & Katch 2001). It is already reported that people with DM have lower Health Adjusted Life Expectancy compared to people without DM (Manuel & Schultz 2004). Objective measurement and quantification of function may reflect the full health of an individual and ultimately contribute to the estimation of healthy life expectancy.

Apart from estimating the functional health of an individual, functional status information has also found a role in care planning, measurement of quality of care and adjustment of payments for case mix under various Medicare prospective payment systems in countries like the USA (Carter, Relles, Ridgeway & Rimes 2003). Considering the value of functional status information in health planning and management, comprehensive evaluation of functional outcome in a chronic condition such as diabetic foot complication would seem essential.

However, it needs to be highlighted at this stage that objective assessment of most of the outcome measures used for comprehensive evaluation of function demands valid measurement tools and the expertise to interpret the findings. In the climate of limited resources for health care, it is difficult to expect the ready availability of both in all clinical settings. Therefore, the purpose of such a comprehensive and multidimensional model of function is to evaluate function in the research setting with the objective of informing clinical services on the problem areas, which require specific attention.

It is evident that management of diabetic foot complications requires a shift of paradigm from intense focussed care following major complications such as LEA to effective management of specific problem areas at the early stages of foot disease. Such an approach may decrease the rate of progression of further complications associated with DMPN resulting in achieving maximal function with cost-effective care. It is already established that providing adequate prevention to all diabetic patients at risk or high risk for foot ulcers and amputations would be a cost-effective or even a cost-saving strategy (Tennvall & Apelqvist 2001).

Early identification of specific problem areas can help to design a purposeful rehabilitation program for diabetic patients with specific needs at consequent stages of foot complications. Thus, a unified multidimensional model of function is necessary to emphasize the comprehensive outlook towards rehabilitation with the objective of maximising functional outcome at consequent stages of foot complications.

2.9: Synopsis of literature review and Null hypotheses

The review of literature indicates that there is a lack of conceptual clarity in the interpretation of functional outcome following diabetic foot complications. Measurement of function has been uni-dimensional in terms of the domains of function. The focus of research in diabetic foot disease is largely on the incidence, causal pathways and mortality. Previous studies have attempted to understand the biomechanical alterations produced by foot complications. However, the available evidence is still incomplete to guide a clear understanding of the mechanisms underlying the changes occurring in the mobility and activity of patients due to diabetic foot disease. Although there are reports on H-RQOL in diabetic patients, the actual capacity and performance of diabetic patients in the presence of foot complications is an entirely new area. Therefore, the need for a comprehensive evaluation of functional outcome in this patient population was deemed essential.

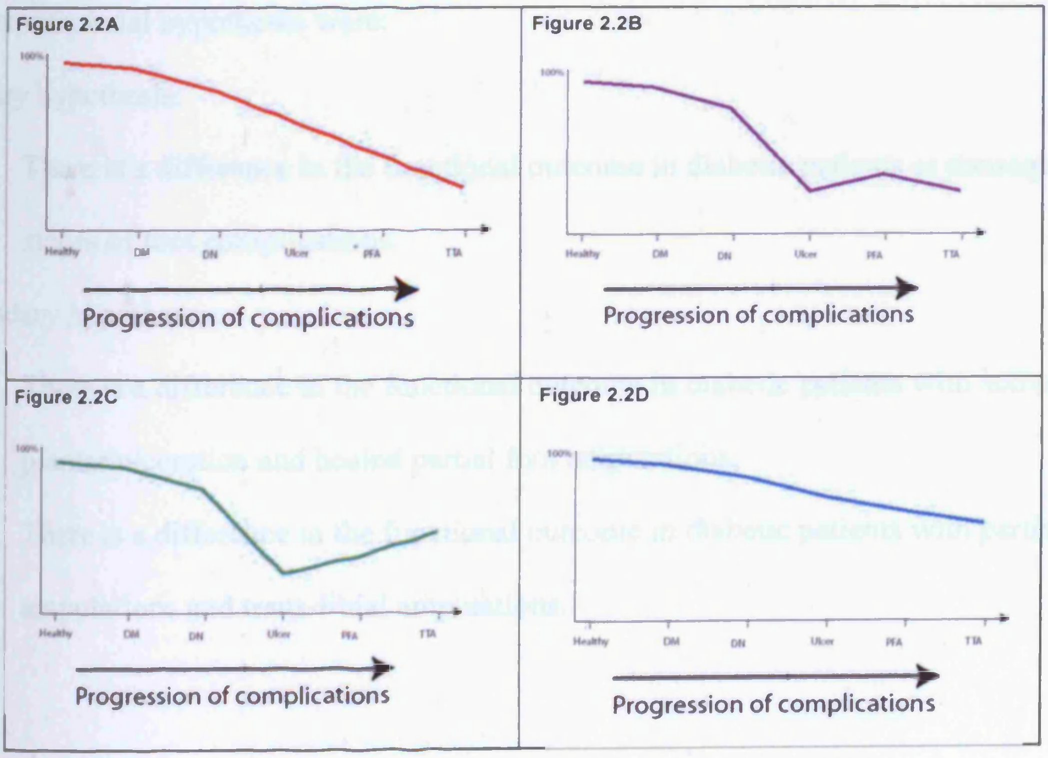
Thus, the present study was designed to explore the nature of the course of functional outcome across four patient groups with diabetic neuropathy at consequent stages of foot complications. It was speculated that patients with diabetic foot disease would demonstrate a decline in the function at consequent stages of foot complications i.e. diabetic neuropathy, diabetic foot ulceration, partial foot amputations and trans-tibial amputations because of the seemingly increasing physical limitations.

Secondly, there is evidence to suggest that diabetic patients with minor amputations are reported to demonstrate better H-RQOL compared to patients with current ulcers (Tennvall & Apelqvist 2000). However, there is lack of evidence to explain the differences in the overall functional outcome between the two groups. Therefore, it was proposed to investigate the differences in functional outcome between the groups with DFU & PFA.

Thirdly, diabetic patients with major lower extremity amputations are reported to demonstrate lower H-RQOL compared to patients with minor amputations (Tennvall & Apelqvist 2000). Moreover, minor amputations such as PFA are often performed in an attempt to salvage the foot for ambulation (Sanders & Dunlap 1992, Mckittrick, Mckittrick & Risley 1993). It is also documented that the more proximal the amputation, greater is the energy cost of ambulation (Waters et al. 1976). However, it is still unclear how the patients belonging to the two groups i.e. PFA (minor or distal level of amputations) and TTA (major or proximal level of amputations) perform in terms of functional outcome. Therefore, it was proposed to compare the functional outcome following the two levels of amputations in diabetic neuropathic patients.

The course of functional outcome following foot complications is unclear at this stage.

Figure 2.2: Possible course of functional outcome following foot complications



It is unclear whether the course shows a steady consistent decline from DMPN to TTA (Figure 2.2A) or whether it dips down with DFU, improves with PFA and drops down with TTA again (Figure 2.2B-purple curve) or whether it dips down with DFU and then improves with PFA and shows further improvement with TTA (Figure 2.2C-green curve).

Hence the null hypotheses were:

Primary hypothesis:

1. There is no difference in the functional outcome in diabetic patients at consequent stages of diabetic foot complications.

Secondary hypotheses were:

1. There is no difference in the functional outcome in diabetic patients with active plantar ulceration and healed partial foot amputations.
2. There is no difference in the functional outcome in diabetic patients with partial foot amputations and trans-tibial amputations.

The experimental hypotheses were:

Primary hypothesis:

1. There is a difference in the functional outcome in diabetic patients at consequent stages of foot complications.

Secondary hypotheses:

1. There is a difference in the functional outcome in diabetic patients with active plantar ulceration and healed partial foot amputations.
2. There is a difference in the functional outcome in diabetic patients with partial foot amputations and trans-tibial amputations.

Chapter 3: Subjects & Methods

This chapter presents the details of the methods used to collect the data for the study. It is structured to include sections namely:

Section 1:

- Ethical approval
- Funding source

Section 2:

- Study design
- Sample size
- Inclusion criteria
- Exclusion criteria

Section 3:

- Recruitment strategy
- Subject cohort

Section 4:

- Data collection
- Data processing and
- Statistical analysis

Section 1:

3.1: Ethical approval:

The study was conducted at the Research Centre for Clinical Kinesiology (RCCK), Department of Physiotherapy, School of Health Care studies, Cardiff University, Heath Park, Cardiff. It was approved by the Cardiff and Vale NHS Trust Research & Development Office and the South East Wales Local Research Ethics Committee. The Trust Research & Development Office, Morriston Hospital, Swansea had approved consent to recruit suitable patients from Morriston Hospital (See copy of the approval letters in Appendix 1). The investigations were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2000.

3.2: Funding source:

The study was funded by the School of Health Care Studies, Cardiff University, Heath Park, Cardiff CF14 4XN. The researcher declares that there were no conflicts of interest.

Section 2:

3.3: Study design:

In this cross-sectional case control study, 4 groups of patients with DMPN were studied. Group A: Controls with DMPN and no history of plantar ulceration (referred to as DMPN group in the text) (n=23), Group B: DMPN with current unilateral plantar ulceration (referred to as DFU group in the text) (n=23), Group C: DMPN with healed unilateral partial foot amputations (referred to as PFA group in the text) (n=16) and Group D: DN with healed unilateral trans-tibial amputations (referred to as TTA group in the text) (n=22). The robustness of this study would increase with a longitudinal design to investigate the variations in functional outcome as the foot complications progress in the diabetic population. However considering the time scale required for a longitudinal study and the cost involved the next feasible option was a cross-sectional study design with strategies such as: 1) Optimal matching of the groups 2) Stringent check on the confounding factors and 3) Cautious interpretation of results.

3.4: Sample Size:

The 4 groups namely: DMPN, DFU, PFA and TTA were compared based on their functional outcome. Minimum sample size was calculated using a standardised difference of 1, a power of 0.8 (α= 0.05). Each group needed a minimum of 23 participants. Gait parameters especially gait velocity is known to be a measure of functional performance (Potter, Evans & Duncan 1995). Moreover, the data for gait parameters was available in the published literature for power calculation. Therefore based on a number of gait parameters reported by Mueller et al. (1994) a range was found for the standardised difference between 1.15 and 1.57 (Mueller et al. 1994). For this power calculation, a conservative estimate of the standard difference of 1 was used.

3.5: Inclusion Criteria:

Known cases of DMPN (diagnosed clinically with 5.07 monofilament) with either no history of plantar ulceration, current unilateral plantar ulceration, unilateral healed PFA and unilateral healed TTA were referred from Podiatry clinics, Diabetic foot clinics and Artificial Limb and Appliance Centres.

Patients in an age group of 40-75 yrs living independently in the community with visual acuity of 20/40 in the better eye (pre-requisite to obtain a driving license) and able to communicate effectively were included in the study. All the participants were able to sit-to-stand and walk independently or with a walking aid for at least 10m. The DFU group included patients with unilateral plantar ulceration. However, patients with ulcers over various plantar sites were included in the study such as fore-foot ulceration and heel ulceration.

The PFA group included patients with healed unilateral partial foot amputations e.g. hallux amputation, ray amputation and trans-metatarsal amputations. The TTA group included patients with healed unilateral trans-tibial amputations.

3.6: Exclusion Criteria:

Patients with amputation levels higher than trans-tibial and those with bilateral lower limb amputations were excluded from the study. Subjects with current manifestations of painful DMPN, neurological and musculo-skeletal impairments apart from those caused by diabetic neuropathy were also excluded. Diabetic patients presenting with painful neuropathy were excluded because patients with severe foot pain are known to have more difficulties when walking long distances than patients with less severe or without any pain (Novak et al. 2004). Those subjects with current manifestations of cardio-respiratory disorders were not included because acute symptoms of cardio-respiratory disorders are likely to have a confounding influence on the energy expenditure of the patients. Patients with neurological and musculo-skeletal impairments (for e.g. hemiplegia, parkinson's disease, multiple sclerosis, symptomatic cases of osteo-arthritis of the hip and knee) apart from those caused by DMPN were excluded to rule out their likely effect on the kinesiological variables (for e.g. standing balance, net joint moments during STS transfer and walking, spatial and temporal parameters of walking and plantar pressure distribution during walking) which would exert a counfounding influence on the findings. In addition, patients taking medication with known effects on the central nervous system, known dependence on alcohol / drugs were excluded to rule out the likely influence on the standing balance of the patients. Patients seeking renal dialysis for renal complications were excluded from the study due to the likely effect on the H-RQOL (Martinez-Castelao et al. 2004).

Section 3:

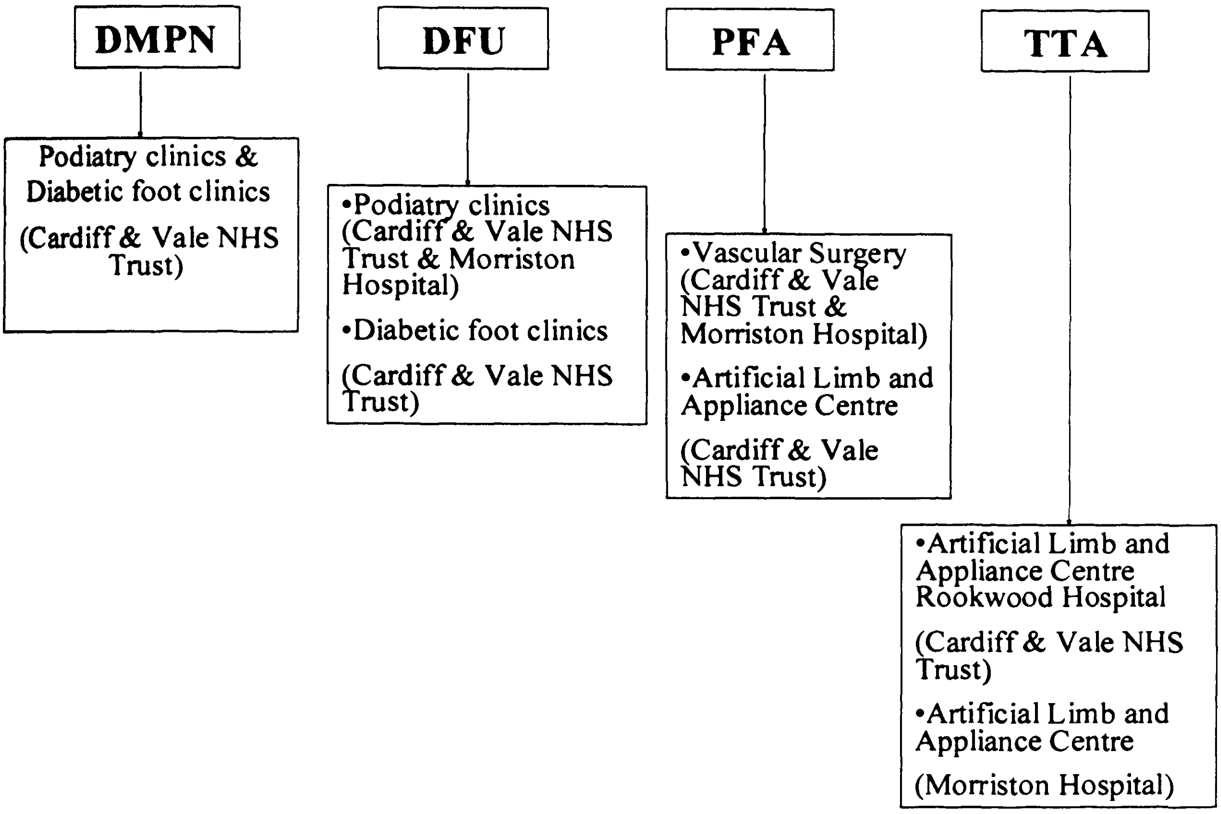
3.7: Recruitment strategy:

Suitable subjects were recruited through the Cardiff & Vale NHS Trust and Morriston Hospital, Swansea. The patients with plantar ulcers and partial foot amputations were identified from Podiatry clinics conducted at Llandough Hospital, University hospital of Wales and Morriston Hospital, Swansea. They were also recruited from the diabetic foot clinics conducted by the Wound Healing Research Unit, Cardiff University, Cardiff. The Departments of Vascular Surgery at the University Hospital of Wales, Cardiff and Morriston Hospital, Swansea identified the suitable subjects with partial foot amputations. Patients with unilateral trans-tibial amputations were recruited from the Department of Physiotherapy and those with unilateral partial foot amputations from the Department of Orthotics services, Artificial Limb and Appliance Centre, Rookwood hospital. The Artificial Limb and Appliance Centre, Swansea also contributed to identifying the patients with trans-tibial amputations.

The recruitment centres within Cardiff and Vale NHS Trust and Morriston Hospital are summarised in the chart below (refer Figure 3.1).

Appropriate subjects were contacted by the respective departments through a letter and an information sheet, which explained the process of the study. A copy of the invitation letter and the information sheet is included in Appendix 1. Potential participants were given a period of minimum two weeks to read and decide whether they wished to participate in the study. They had the choice to refuse to participate in the study and that did not affect their treatment in any way. The Research Assistant from the Research Centre for Clinical Kinesiology (RCCK) contacted them over the telephone to know their decision. Those patients who agreed to participate were asked simple questions pertaining to their past and present health status to ensure they were eligible to participate in the study (Screening questionnaire is attached to the Appendix 1). On receiving this basic information, an appointment was fixed based on the time feasible for the RCCK and the subject. Transport was arranged for those subjects who were unable to find their own transport to and from the RCCK. Those using their own transport were helped with the parking facilities at UHW, Cardiff. Subjects requiring help to reach the RCCK from the parking area were either escorted or transferred in a wheelchair depending on their requirement.

Figure 3.1: Recruitment centres within Cardiff and Vale NHS Trust and Morriston Hospital



On reaching the RCCK, the participant was made comfortable and given sometime to relax before the beginning of data collection. Each participant was required to sign an informed written consent sheet (Consent sheet attached to the Appendix 1). The entire assessment was completed in a single visit over a period of approximately two hours.

3.8: Subject cohort:

As determined by the power calculation minimum number of subjects (minimum=23) were included in three groups namely: Group DMPN n=23, Group DFU n=23 and Group TTA n=22. Considering the stringent inclusion and exclusion criteria defined for the present study the recruitment of the 4 groups was a challenging task which continued over a period of 20 months. The most difficult group to recruit was the group of subjects with unilateral healed PFA. To illustrate the difficulties in recruitment the following examples are provided.

Patients from the two major NHS Trust Hospitals and three Podiatry and two diabetic foot Clinics were screened for recruitment. At the one hospital, 32 subjects underwent PFA over a 2-year period. PFA was performed as a primary procedure on 25 (25/32) subjects, of those 9 had diabetes (DM). One (1/9) subject attained healing, 6 (6/9) subjects with DM did not heal until July 2005 & 2 subjects underwent ipsi-lateral TTA (76 & 80 wks respectively) later. Seven (7/32) subjects underwent PFA as a secondary procedure (the primary procedure in these patients was vascular reconstruction) and out of those 4 subjects had DM; of those 4, 3 subjects did not heal & one did not wish to participate in the study.
At the second hospital, 18 patients with diabetes related PFA were identified of which 2 subjects remained unhealed, 4 subjects developed contra-lateral LEA following PFA, 6 subjects developed ipsi-lateral plantar ulceration following PFA, 1 subject was severely affected by Osteoarthritis, 1 subject suffered from partial blindness and 4 subjects did not respond to the invitation. Effectively, between the two hospitals from the 50 patients identified over a 19-months period, one ended up participating in our study. Another 15 subjects with healed PFA were identified through the various clinics.

This challenging recruitment process highlights the difficulty in finding diabetic subjects with unilateral PFA that are healed, which was a requirement for this kinesiology study. This could be attributed to many factors:

(1) Very low incidence of PFA compared to major LEA among diabetic subjects in South Wales: Findings from the clinical audit (unpublished data) demonstrate a lower incidence of foot amputations (13.9%) compared to major amputations (86.1%) in the South Wales region over a two-year period. Rayman et al. (2004) have reported a lower incidence of minor amputations (43.0%) compared to major amputations (57.0%) in a prospective study conducted in the UK (Rayman, Krishnan, Baker, Wareham & Rayman 2004). Another study conducted in America has also demonstrated a lower rate of partial foot amputations (34.9%) compared to leg amputations (65.1%) in diabetic patients (Most & Sinnock 1983).

(2) Prolonged period of wound healing demonstrated by diabetic subjects following PFA. Our subject from the hospital had a healing time of 24 wks. Unfortunately, we did not have this information for the other 15 participants. The reported average healing time is 29 wks, range 3-191 wks (Larsson et al. 1998). The incidence of multiple problems e.g. skin breakdown, wound failure or higher amputation levels following foot amputations e.g. trans-metatarsal amputations among diabetic people (Mueller, Allen & Sinacore 1995) would explain the low number of patients with healed PFA.

(3) The experience with recruitment of the subjects confirms the previously reported findings stating that diabetic patients with PFA present with an increased risk for ulceration and re-amputation (Armstrong et al. 1997). Of the 27 diabetic subjects from both the centres 22.2% underwent re-amputation (2/27 ipsi-lateral amputations, 4/27 contra-lateral amputations) and 22.2% of subjects developed ipsi-lateral plantar ulceration.

Kinesiological studies involving people with PFA require complete healing following an amputation. The presence of a wound could confound the results since it can produce movement alterations in addition to the ones already produced by PFA. Because of the difficulties encountered during the recruitment process the researcher had to settle with less than 23 subjects in the PFA group (n=16) and the TTA group (n=22).

At the stage of statistical analysis, 2:1 matching was performed for the PFA group subjects whereas analysis of the TTA group did not require any further action.

3.9: Audit:

This audit was inspired by the difficulties encountered during the recruitment of the subjects for the 4 groups in the present study. During this study, the question arose about the frequency and timing of repeated amputations, which could explain the cause for the unavailability of such subjects for the study. Despite the disconcerting rate of re-amputations among the diabetic population, there is limited literature available to evaluate the current status of re-amputation in these subjects. Therefore, a retrospective study (clinical audit) was conducted to investigate the incidence of re-amputation following diabetes-related lower extremity amputations (LEAs) among patients referred for rehabilitation in South Wales, UK.

Manual and electronic data gathering systems were used to record the patient information from the two Artificial Limb & Appliance Centers providing services to South Wales. The data included demographic information, causes of amputation, occurrence of various levels of re-amputation and grades of mobility score.

The results of the study were as follows:

During a two-year period (2001-2003), 473 people with LEAs resulting from various causes were referred to the two centres. Two hundred and five subjects with DM underwent 316 amputations, of which 44 were foot amputations and 272 major amputations on the ipsilateral and contra lateral sides. More than forty-five percent (45.85%) of the diabetic population with single LEA underwent re-amputations with 28.29 % incidence of contra lateral LEA within two years compared to 23.13% of non-diabetic dysvascular population.

The ipsilateral re-amputations occurred much earlier (within 3 months) compared to the contra lateral amputations which took 10 times longer (within 30 months) following the first event of LEA. Subjects with DM scored lower on the mobility score compared to the non-diabetic dysvascular subjects.

Based on our results we inferred that DM emerges as the leading cause of LEAs among patients referred for rehabilitation in South Wales, UK. The incidence of re-amputation is highest among the diabetic patients though the progression of events does not follow a particularly consistent sequence on the ipsilateral or the contra lateral side. Co-morbid causes associated with DM might explain the significantly lower scores of mobility among the diabetic amputee population. Regular evaluation of the incidence of re-amputations in this patient population in the form of nationwide epidemiological studies is necessary to explore the effectiveness of the continued treatment care and improve it for better functional outcome.

Section 4:

3.10: Methods of Data Collection:

The entire assessment process is classified into Part I, which includes preliminary examination, and Part II, which includes specific measurement of the outcome measures of function.

Part I: Preliminary examination

Table 3.1 presents the key preliminary parameters and the general information recorded during the preliminary examination of the subjects.

Table 3.1: General examination and key preliminary parameters

General examination	Personal details
	Demographic information
	Diabetes related information
	Past medical and surgical history
	Amputation related information
	Ulcer related information
	Visual acuity
	Blood pressure
Key preliminary parameters	Range of motion
	Muscle strength
	Blood glucose

Preliminary examination included recording of relevant personal details of the patient along with demographic information. The type of DM and the time duration since the onset of DM was recorded. Duration of DM relied totally on the patient's memory, as they did not have a specific record card mentioning the date of diagnosis of DM. Information pertaining to past medical and surgical history was obtained with specific emphasis on cardiac and respiratory disorders. Despite screening the patients for gross musculo-skeletal and neurological disorders other than DM before their participation in the study, any such disorder was ruled out during the history taking process. Information regarding the side and the level of amputation was recorded in patients belonging to PFA and TTA groups. In the DFU group patients the side and site of plantar ulceration was recorded. The patients belonging to the DFU group were questioned to note the instructions given to them regarding weight bearing (refer to assessment sheet in Appendix 1) with the purpose of interpreting their performance of walking.

In addition, visual acuity, blood pressure, range of motion of the lower extremity joints, lower extremity muscle strength and blood glucose levels. The objective of this assessment was to conduct a comprehensive examination and rule out the presence of any confounding factors, which might influence the findings of the study since DM, is a multi system disorder (Holmboe 2002).

3.10A: Visual acuity:

Considering the high prevalence (64.1%) of diabetic retinopathy among diabetic patients (Al Till, Al Bdour & Ajlouni 2005) visual acuity was assessed to confirm that the subjects did not suffer from partial or complete blindness. Loss of visual input is known to decrease stability in standing (Raymakers, Samson & Verhaar 2005) and therefore people with partial or complete blindness were excluded to avoid bias in the interpretation of the results of posturography. Visual acuity was confirmed using the Snellen chart at a distance of 3 meters. None of the participants of the present study presented with blindness.

3.10B: Blood Pressure:

The patients were tested for orthostatic hypotension. The resting blood pressure was measured using the OMRON Automatic Oscillometric Digital Blood Pressure Monitor

(OMRON, Model HEM-705 CP) (O'Brien 1996) in the supine and standing position to check for orthostatic hypotension (drop of >20mmHg in systolic pressure or a fall of > 10mmHg in diastolic pressure) (Dey & Kenny 1998).

3.10C: Range of motion (ROM) and Deformities:

The range of motion of the hip, knee, ankle and foot was measured to rule out any gross limitation in the range of motion resulting from any other neuro-musculokeletal disorders apart from DM. The range of motion of the hip, knee, ankle and the 1st metatarso-phalanegal joint in the sagittal plane was recorded using a Digital Video camera. siliconCOACH pro version-6 was used for the calculation of the joint angles in two dimensions by digitising the markers on the anatomical landmarks (Elliott et al. 2002). The range of motion in the sagittal plane was recorded as the angle between the starting position and the end position of the movement at the hip, knee, ankle and 1st MTP joint as demonstrated in Table 3.2 and Figures 3.2.

Anterior, posterior, lateral and medial views of the foot were photographed to identify the medial longitudinal arch of the foot. In the interpretation of the plantar pressure distribution it was necessary to note the distribution of patients with obliteration of the arch between the groups. Patients with Charcot foot were excluded from the study as mentioned before.

Table 3.2: Joint angle measurement for the hip, knee, ankle and 1st MTP joint

Joint	2 arms of the angle	Starting position	End position
Hip	**Arm 1:** between the greater trochanter of the femur and the lateral epicondyle of the femur **Arm 2:** long axis of the trunk passing through the greater trochanter	Supine: Hip neutral	Supine: Maximal hip flexed
Knee	**Arm 1:** between the greater trochanter of the femur and the lateral epicondyle of the femur **Arm 2:** between the lateral epicondyle of the femur and the lateral condyle of the fibula	Supine: Knee neutral	Supine: Maximal knee flexed
Ankle	**Arm 1:** between the head of the fibula and the lateral condyle of the fibula **Arm 2:** along the long axis of the foot on the lateral border of the foot	Supine: Ankle neutral	Supine: Maximal ankle dorsiflexion and plantarflexion
1st MTP	**Arm 1:** along the long axis of the 1st metatarsal on the medial border of the foot **Arm 2:** along the long axis of the first phalanx of the hallux	Supine: 1st MTP joint neutral	Supine: Maximal 1st MTP joint dorsiflexion and plantarflexion

Figure 3.2: Composite picture of ROM measurement

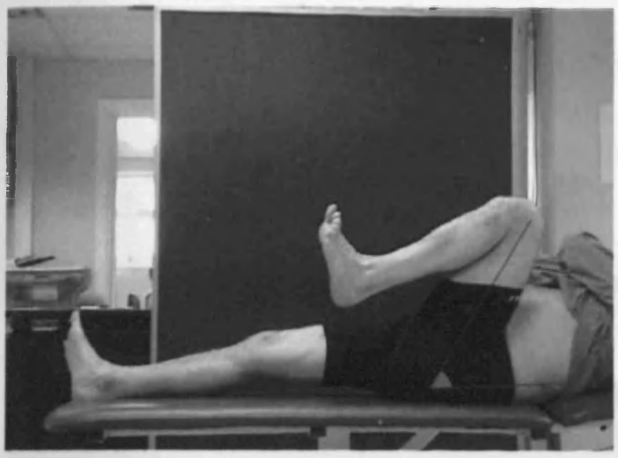
A: Measurement of ROM at the right hip joint using siliconCOACH software

B: Measurement of ROM at the right knee joint using siliconCOACH software

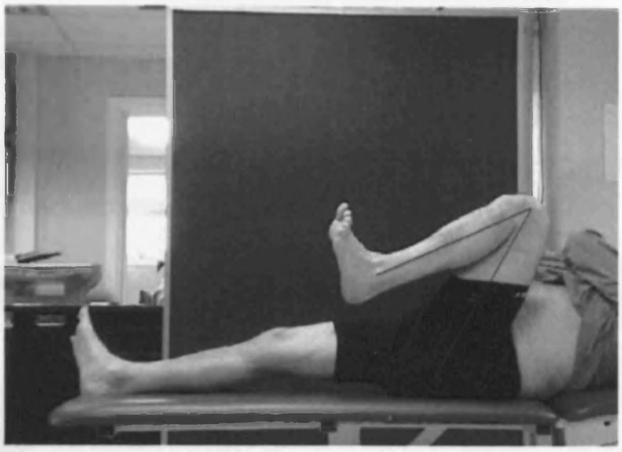
C: Measurement of ROM at the right ankle joint using siliconCOACH software

D: Measurement of ROM at the right 1st MTP joint using siliconCOACH software

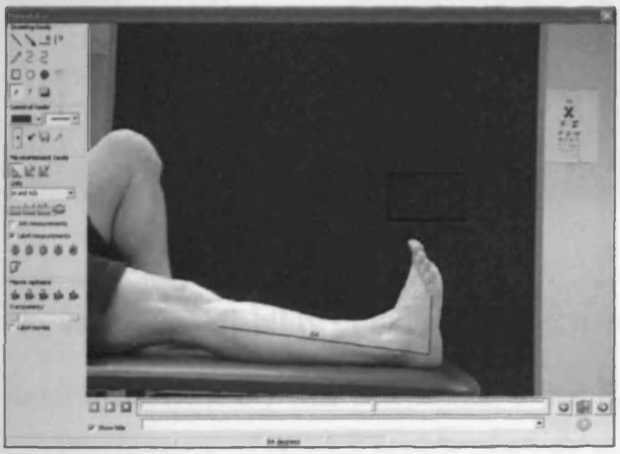
A: Hip ROM



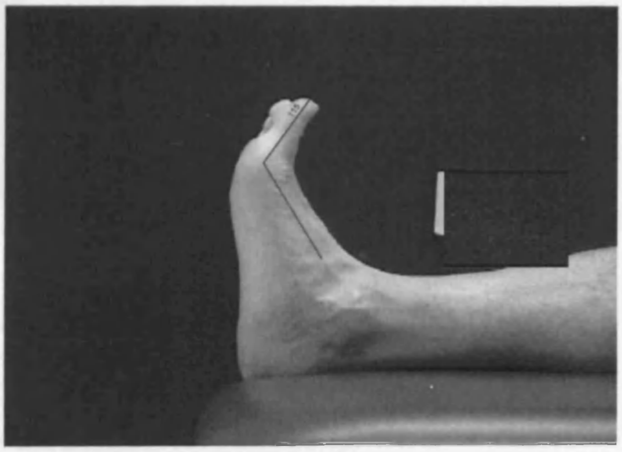
B: Knee ROM



C: Ankle ROM



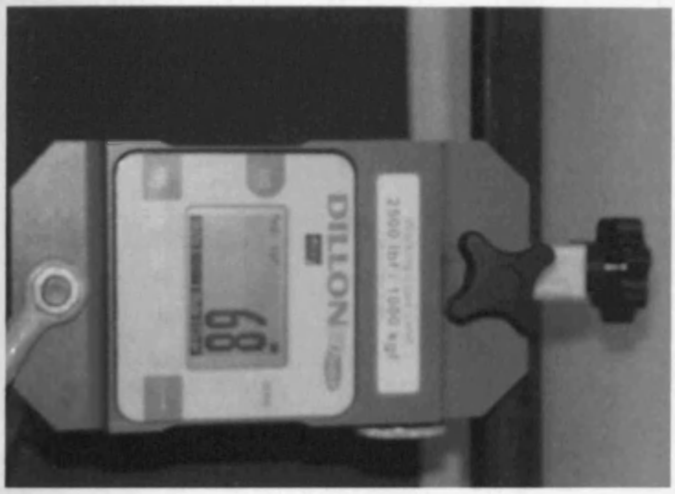
D: 1ST MTP ROM



3.10D: Muscle strength:

Dynamometry was used to identify gross impairments in muscle strength (Bohannon 2005) other than those caused by DM. In the present study, gross impairment in muscle strength was defined as inability to complete the full range of joint motion actively which is classified as grade 3 on the Oxford scale for assessment of muscle strength. Muscle strength for individual muscle groups was measured using the Johnson Scale DILLON ED junior dynamometer (EDjr) (Dillon/Quality Plus, Inc.Camarillo, CA) (refer Figure 3.3). The force developed by the hip flexors, extensors, abductors, adductors, knee flexors and extensors and ankle dorsiflexors and plantarflexors was measured in kilogram-force (kgf).

Figure 3.3: Johnson Scale DILLON ED junior dynamometer (EDjr) fixed to the wall. The force developed by the muscle was measured in kilogram-force (kgf).



The intratester reliability of the measuring instrument (Johnson Scale, model DILLON ED junior dynamometer) was determined at the RCCK for hip extensors and abductors, knee flexors and extensors, and ankle dorsiflexors and planterflexors on 10 healthy subjects with 3 measurements for each muscle group (Fallatah 2005). All the muscle groups showed excellent reliability and the ICC values for each muscle group for the right and the left lower limb were similar (Right lower limb: ankle dorsiflexors=0.954, ankle plantar flexors=0.943, knee flexors=0.927, knee extensors=0.929, hip extensors=0.961, hip abductors=0.963) (Fallatah 2005). The point of application of the resistance was always perpendicular to the long axis of the limb. Muscle force was measured during static contraction for each muscle group and 3 trials were recorded with a rest period of one minute between each muscle group. The test protocol and the test positions in the reliability study and the present study were the same (refer Figure 3.4). The test positions for the various muscle groups are presented in the Table 3.3. The muscle strength for the ankle dorsiflexors and plantarflexors was not tested on the affected foot of the patients belonging to the DFU group and PFA group.

Table 3.3: Testing positions for various lower extremity muscles

Joint	Muscle groups	Starting position	Point of application of resistance	Muscle action
Hip	Flexor	Standing in front of the dynamometer holding the pole*	Lower 1/3rd of the thigh	Forward flexion of the hip maintaining an erect trunk posture
	Extensor	Standing with the back facing the dynamometer holding the couch*	Lower 1/3rd of the thigh	Extension of the hip maintaining an erect trunk posture
	Abductor	Standing beside the dynamometer holding the couch*	Lower 1/3rd of the thigh	Abduction of the hip maintaining an erect trunk posture
	Adductor	Standing beside the dynamometer holding the couch*	Lower 1/3rd of the thigh	Adduction of the hip maintaining an erect trunk posture
Knee	Flexor	Sitting on the couch facing the pole*	Lower 1/3rd of the leg	Flexion of the knee
	Extensor	Sitting on the couch with the back facing the dynamometer *	Lower 1/3rd of the leg	Extension of the knee
Ankle	Dorsiflexor	Long sitting position on the couch with erect back supported by the backrest	Distal half of the foot	Dorsiflexion of the ankle
	Plantarflexor	Long sitting position on the couch with erect back supported by the backrest	Distal half of the foot	Plantarflexion of the ankle

Pole*: The dynamometer was fixed to the pole secured to the wall.

Couch*: The couch was arranged for support while performing the muscle action. The height of the couch was arranged to the patient's height such that they did not have to bend from the trunk.

Figure 3.4: Test positions for hip, knee and ankle muscle strength

A: Hip adductors

B: Knee extensors

C: Knee flexors

D: Ankle dorsiflexors

E: Ankle plantarflexors

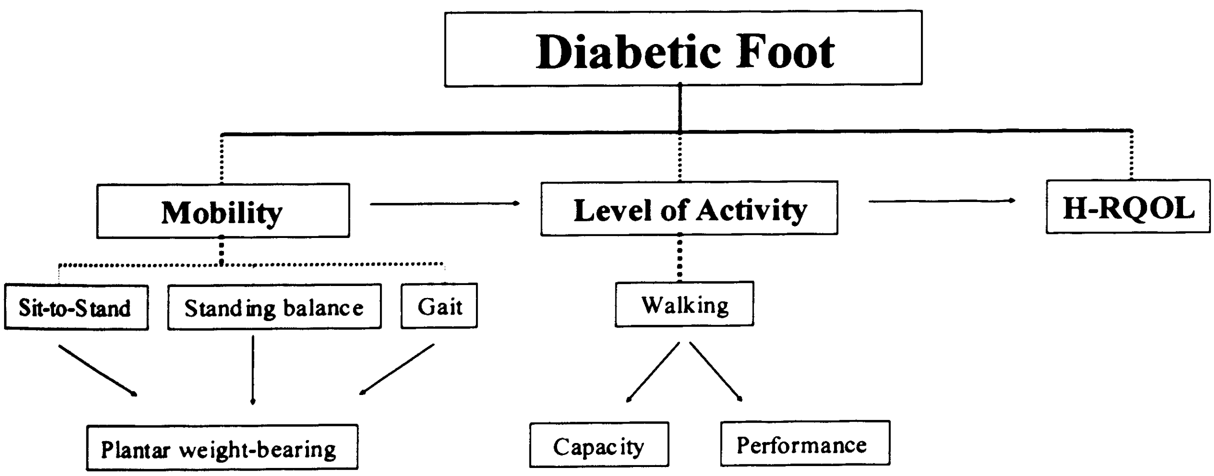
3.10E: Blood Glucose:

Blood glucose level was measured using MediSense- Precision Q.I.D, Blood glucose sensor (Abbott Diagnostic Division, Maidenhead, Berks SL6 3EZ). The patient was comfortably seated in a chair with the left elbow supported with a pillow and the left hand supported over the table. The Physiotherapist (tester) trained for this procedure performed the measurement with gloved hands. Necessary hygienic precautions were taken and safety procedures were strictly adhered to. The measurement involved a prick over the tip of the left middle finger with the instrument. Disposal units were used to avoid any cross contamination of blood. A strip was used to measure the blood glucose level and the value was recorded in the patients assessment form for record. The NHS regulations were strictly adhered to while disposing the sharps utilised for the procedure. Hypoglycemic (< 4.5 mmol/ l) patients were provided with adequate glucose tablets to increase the glucose levels to optimum and the measurement was repeated to ensure optimal blood glucose level before proceeding with further assessment.

Part II: Measurement of outcome measures used to compare the functional outcome

This part includes the measurement of the various outcome measures selected to assess different domains of function beginning with assessment of DMPN. Functional outcome was measured in four primary domains: Impairment, Mobility, Activity level and Participation / H-R QOL (refer Figure 3.5).

Figure 3.5: Proposed model of functional outcome



3.10F: Impairment: Peripheral neuropathy:

The subjects recruited for the study were already clinically established cases of DMPN. Touch pressure sensation using the Semmes-Weinstein monofilament was tested to confirm the presence of DMPN in these patients. Testing the presence or absence of vibration sensation with a tunning fork was used only to corroborate the findings from S-W filament testing.

3.10G: Touch pressure sensation:

A Semmes-Weinstein monofilament was used to confirm the neuropathy status. S-W monofilament is known to be a valid and reliable clinical tool to test for peripheral neuropathy (Kumar, Fernando, Veves, Knowles, Young & Boulton 1991). The S-W monofilament is a set of 20 pressure-sensitive nylon filaments attached to a penholder. Each monofilament is a piece of nylon line of a precise diameter that is applied end-on-to the skin until the line begins to bend (refer Figure 3.6), providing a reproducible, metered sensory stimulus (Guyton & Saltzman 2001).

The level of sensation produced by 5.07 monofilament is regarded as the level of sensation protective against foot ulceration (Olmos et al. 1995). DMPN was defined neuropathy as inability to perceive the 5.07 (10gm) Semmes-Weinstein monofilament (loss of protective sensation) (Birke & Sims 1985) in at least one of the 4 plantar areas tested for this study.

Figure 3.6: Testing the touch pressure sensation with a 10 gm S-W monofilament over the head of the 1st metatarsal

The four sites tested in the crook lying position were: heel, 1st metatarsal head, 5th metatarsal head and hallux. Five to 10 trials were performed at each site (Diamond et al. 1989) and the subject needed to perceive 80% of the trials to be graded as the sensation present over that site. The site was scored 1 in case of presence of sensation and 0 in case of absence of the sensation. The sum of the scores over the 4 sites was used to present the final sensory score over the entire foot. Prior to testing the sensation over the four plantar sites the patient was given a feel of the touch pressure sensation over the centre of the forehead.

3.10H: Associated sensory assessment: Vibration perception

In addition to the primary sensory testing conducted using the the S-W monofilaments to confirm the peripheral neuropathy, vibration sense was tested over the feet to supplement the information recorded by sensory testing. A tunning fork was used to assess the vibration sense (128 Hz) (Meijer et al. 2005) over the medial aspect of the head of the 1st metatarsal except in patients with PFA where the sensation was tested over the most distal bony prominence of the residual foot. The examiner struck the tunning fork against the palm so that the vibration could be felt and then demonstrated the sensation over the patient's ulnar styloid before testing it over the foot. The presence or loss of the sensation was recorded with one attentive trial as 1 or 0.

3.10I: Mobility: Performance-based measures:

3.10J: STS analysis:

Quantitative analysis of the STS movement was performed using the technique of inverse dynamics (van Deursen 2005). The word 'inverse' indicates that the causes of movement (forces and moments) are calculated from the outcome (movement as it is measured). The aim of such an analysis is to determine the forces and moments at the different joints particularly the net joint forces and net joint moments during movement. In the present study the movement of STS was analysed in terms of the four phases of STS, the net joint moments around the hip, knee and ankle and the symmetry of the movement in terms of weight-bearing. The four phases of the sit-to-stand movement studied were: 1) Forward flexion, 2) Seat off, 3) Maximum ankle dorsiflexion and 4) End hip extension (Schenkman et al. 1990). The parameters considered for analyses were: 1) Time taken to complete full extension, 2) Time to attain stability, 3) Net joint moments around the hip, knee and ankle & 4) Symmetry of the movement in terms of weight-bearing. Each of these 4 parameters is described below as the kinetic and kinematic analysis of the movement is explained.

Kinematic analysis of the STS movement included the measurement of maximum dorsiflexion of the ankle joint with reference to the ground indicating the initiation of the movement and the highest position of the centre of the pelvis in space during the movement indicating full extension. Full extension was defined as the time taken in seconds from initiation to complete extension during the STS task.

Kinetic analysis included the recording of the seat off which was identified with the force platform when the weight was removed off the seat. The excursion of the Centre of Pressure (COP) was recorded by the force platform from the time of intiation of STS movement upto the point of full extension and beyond to the point of attainment of stability. Time to stability was interpreted as the excursion of the COP during the phase of stabilisation after the phase of full extension of the STS. The COP excursion during quiet standing was used as a reference to determine the time to stability during the STS. The time to stability calculated during STS can be considered as a measure of dynamic stability in terms of balance.

Matlab software (The Mathworks, Inc; Version 6.5 Release 13, 2002) was used to compute the time taken to attain the 4 phases in sec and the maximum net joint moments in Newton.meter (N.m) around the hip, knee and ankle bilaterally during the movement of rising from the chair.

Sit-to-stand movement was analysed using the Kistler force platform (Kistler 925 3A12 Multi-component force plate; Kistler instruments Ltd; Alresford House, Mill Lane, Alton, Hampshire, GU34 2QJ, UK) along with Vicon 512 system (Vicon Motion Systems, 14 Minns Business Park, West Way, Oxford, OX2 OJB, UK) and 8 high resolution infrared (LED strobe lights fixed around the lens) cameras (JAI 50 Hz) to collect the kinetic and kinematic data. The Vicon 512 system is known to be a reliable method to analyse the sit-to-stand movement (van Deursen, Busse & Wiles 2003).

Prior to recording the data, anthropometric measurements were taken as described below.

3.10K: Anthropometric Measurements and Calibration procedure:

Height, body mass, thigh length, leg length, foot length, ankle width, knee width & knee height were recorded in standard units of metric system. Standing height was measured in centimeter with the subject standing erect facing the back to the measuring scale, looking straight ahead using Seca 222 telescopic wall mounted measuring rod (Seca Ltd, Medical scales and measuring systems, 40 Bran Street, Birmingham B5 5QB, UK). Height was converted to meter for analysis of results. Body mass was measured in Kilogram using a digital weighing scale (Seca 888 digital weighing scales; Seca Ltd, Medical scales and measuring systems, 40 Bran Street, Birmingham B5 5QB, UK). Height and the body mass were measured with the uniform standard footwear i.e. Pullman shoes (Thamert [UK] Ltd, Banbury, Oxon). All the subjects wore the same shoes during the process of data collection.

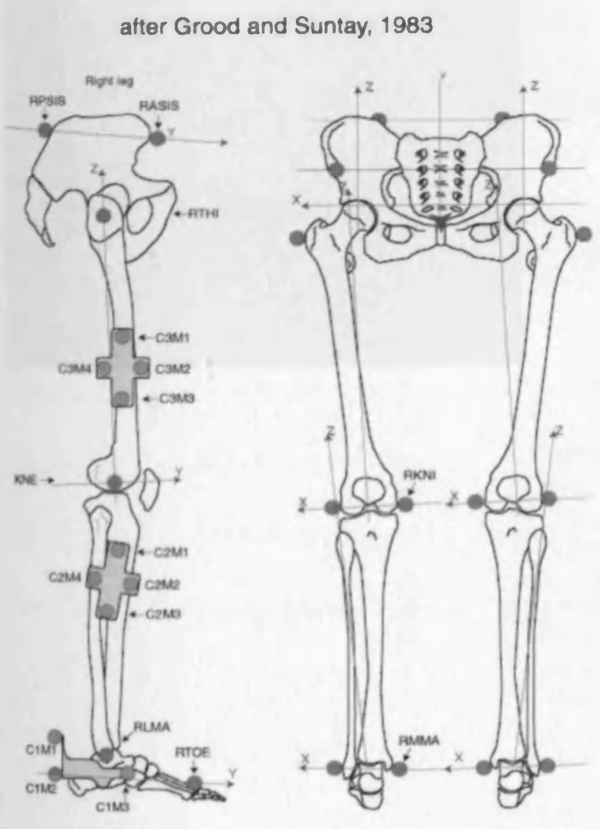
The required anthropometric measurements were taken before the data collection (refer Table 3.4). Linear measurements were recorded in centimeter with a non-stretchable measuring tape (RS Components, P.O. Box 99, Corby, Northants, NN17 9RS, UK). In addition to the foot length, the knee and ankle joint width was measured in cm using a vernier calliper (RS Components, P.O. Box 99, Corby, Northants, NN17 9RS, UK).

Reflective markers were taped to well-defined anatomical sites (Grood & Suntay 1983) namely: bilateral acromion process, bilateral anterior superior iliac spines, bilateral posterior superior iliac spines, bilateral greater trochanter, bilateral medial epicondyle and bilateral knee joint line, bilateral medial malleolus and lateral malleolus and 2nd metatarsal head (refer Figure 3.7).

Table 3.4: Anthropometric measurements

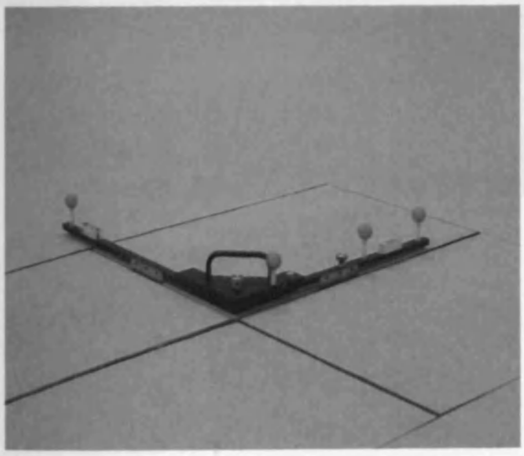
Anthropometric measurement	Groups: DMPN+DFU+PFA	Group: TTA	Position
Thigh length	From the greater trochanter to the lateral epicondyle of the femur	From the greater trochanter to the lateral epicondyle of the femur	Supine
Foot length	From the posterior edge of the heel to the most distal point of the toes	The prosthetic foot length	Sitting
Ankle width	Between the two malleoli	Prosthetic ankle width	Sitting
Knee width	Between the two epicondyles	Prosthetic knee width	Sitting
Knee height	From the lateral knee joint line to the floor with the tibia perpendicular to the floor	Marking a point on the prosthetic limb corresponding to the knee joint line on the contra lateral side	Standing

Figure 3.7: Anatomical sites defined by Grood & Suntay 1983 to place the reflective markers (with thanks to Dr. RWM van Deursen, 1999)



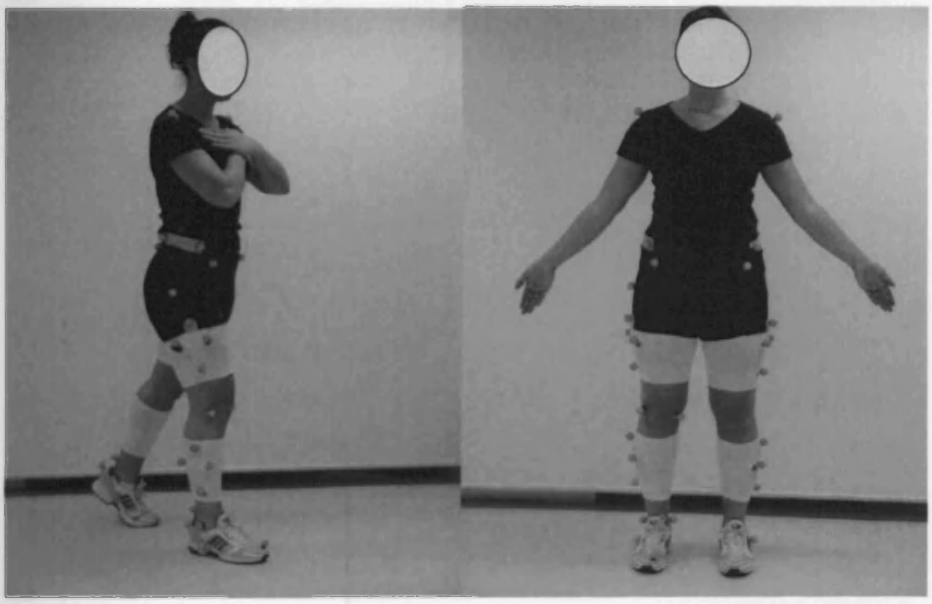
As the subject moved through the capture volume, light from the strobes was reflected back into the camera lens and struck a light sensitive plate creating a video signal. The Vicon datastation collected these signals along with the analogue signals from the force plates for further analysis of movement. Prior to the data collection session, the data acquisition volume of Vicon 512 system was calibrated. Calibration allowed the system to define the capture volume and the relative positions and orientation of the cameras. Static calibration was used to set the origin and direction of the axes. Dynamic calibration was used to calculate the relative positions and orientation of the cameras. Static and dynamic calibration was used to ensure the accurate positioning of the cameras with respect to the corresponding displacement of the reflective markers in the data acquisition system volume (Figure 3.8).

Figure 3.8: Static (top left) and dynamic calibration (bottom right)



The anatomical calibration and anatomical position were recorded with the reflective markers to determine the local co-ordinates of the anatomical landmarks relative to the marker sets which were used during the sit-to-stand movement trials (refer Figure 3.9).

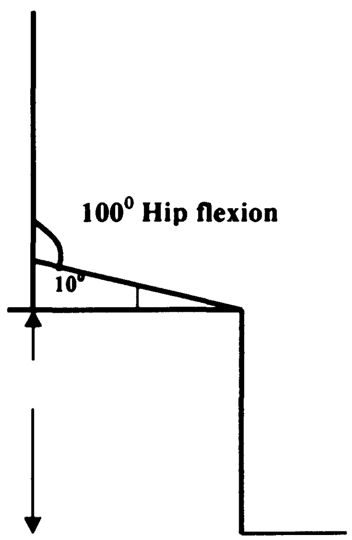
Figure 3.9: Anatomical calibration (left) and anatomical position (right)



The subject was sitting on a height-adjustable chair without any arm or back support (RH Support Froli; RH Form, Upper Tulse Hill Trading Estate, 5 Somers Place, London SW2 2AL UK) placed over the force platform with reflective markers placed on the bony prominences defined above (refer to Figure 3.7).

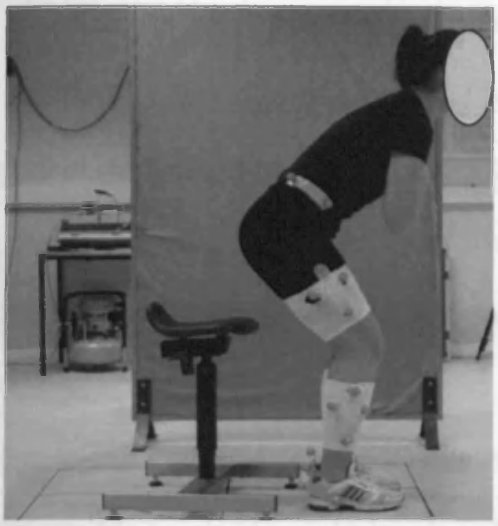
The chair height was determined for individual subject such that the hip was flexed to 100 deg of flexion during sitting and the ankle positioned in neutral position with the feet placed parallel to each other (refer Figure 3.10). The height of the chair was calculated using the formula: knee height + (thigh length (distance from the greater trochanter to the lateral epicondyle of the femur) * sin 10 deg =0.1763) to ensure accurate position of the chair for each subject.

Figure 3.10: Determination of the chair height



The chair height is known to influence the moments of the joints during rising from the chair (Rodosky, Andriacchi, & Andersson 1989). The joint moments are known to increase with decreasing chair height (Rodosky, Andriacchi & Andersson 1989). Therefore considering the ease in the performance of the movement the chair height was adjusted such that the hip was positioned in 100^0 flexion.

Figure 3.11: Sit-to-stand movement recorded



The subject was instructed to place the feet parallel to each other in front of the chair and rise from the seat in a natural manner similar to their daily execution of the task. They were asked to position both the upper limbs in front of the trunk as far as possible to allow uninterrupted visibility of the hip markers during the trial (refer Figure 3.11). Three trials were recorded and the average of the three trials was computed for further analysis (van Deursen, Busse & Wiles 2003). The raw data collected from sit-to-stand movement trials were reconstructed and labelled before it were analysed with the Matlab software programmes. Matlab software (The Mathworks, Inc; Version 6.5 Release 13, 2002) was used to compute the time taken to attain full extension in sec, time taken to attain stability in sec, maximum net joint moments in Newton.meter (N.m) around the hip, knee and ankle bilaterally and the symmetry of weight-bearing during the movement of rising from the chair. It needs to be specified that the maximum joint moments would have occurred at different stages of the STS task performance.

The method for automatic phase determination of STS used in the present study was tested for reliability previously (Busse 2004). Ten healthy subjects were studied with the mean age of 41.1 yr (age range=22-77 yr). The results of the study demonstrated greater variability with respect to seat off and time to stability (ICC=0.33 & ICC=0.36 respectively) due to the variability executed by the subjects in the performance of the task. Therefore, an average of three trials was calculated.

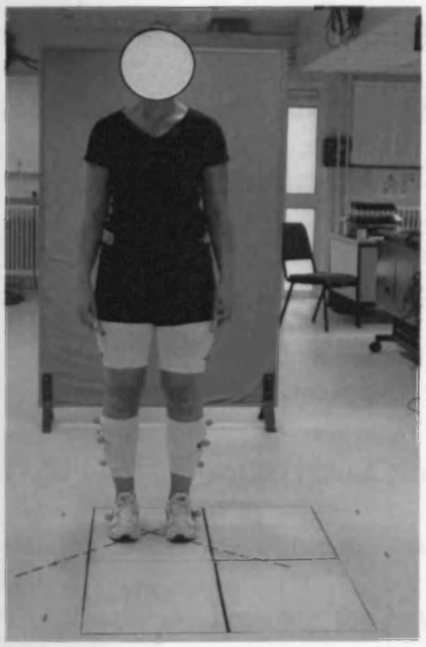
In addition to the net joint moments during the STS task, the symmetry of performance was assessed in terms of weight-bearing. The symmetry of weight-bearing was measured to test the effect of unilateral foot complications on the symmetry of performance of the task. The position of the COP between the two ankles was used as an indicator of symmetry. The value of weight-bearing would be 50% if the COP was exactly in the middle of the area between the two ankles. If the weight-bearing value was more than 50% it indicated that the patient took increased weight on the right side of the body. If the weight-bearing value was less than 50% it indicated that the patient took increased weight on the left side of the body. Based on the information noted regarding the affected and the unaffected side it was determined whether the patient transferred the body weight on the affected or the contra-lateral lower limb while rising from the chair.

3.10L: Standing Balance (Quiet Standing):

Quiet stance has been used to assess the human postural control during upright stance (Hsiao-Wecksler, Katdare, Matson, Liu, Lipsitz, & Collins 2003). In the present study, it was assessed using static posturography wherein the motion of the COP is measured as the subject quietly stands on a force platform (Panzer, Bandinelli & Hallett 1995).

The Kistler force platform (Kistler 925 3A12 Multi-component force plate; Kistler instruments Ltd; Alresford House, Mill Lane, Alton, Hampshire, GU34 2QJ, UK) connected to an eight channel amplifier and A-D converter was used to record the ground reaction forces. The raw signals were processed on a computer. Matlab software (The Mathworks, Inc; Version 6.5 Release 13, 2002) was used to compute the excursion of COP trajectory in meter as an indicator of postural sway and stability over a period of 30 sec.

Figure 3.12: Standing balance recorded during quiet standing on a force platform



Subjects were asked to stand still on a force platform for a period of 30 seconds (Hermodsson et al. 1994) and the excursion of the centre of pressure (COP) trajectory was measured in meter. The COP is the point of application of the resultant of the vertical ground reaction forces (Viton, Mouchnino, Mille, Cincera, Delarque, Pedotti, Bardot & Massion 2000) which was determined from the force platform. The subjects were instructed to stand with their eyes open & feet placed parallel to each other at a distance of approximately 20cm and place the upper limbs by the side of the body while looking straight ahead (refer Figure 3.12). All the subjects used the uniform standard footwear for this measurement. Three trials were recorded and the average length of the COP trajectory was considered for further analysis to attain as accurate results as possible (Ekdahl, Jarnlo & Andersson 1989).

The basic assumption is that the position of the COP represents the vertical projection of the COG on the transverse plane; the path about this COG point is frequently called the sway path. It is presumed that increased postural sway as measured by the total sway path represents decreased stability. Since the force platform directly measures the acceleration to obtain the COP an increase in the amount of sway may indicate either postural control deficits or adoption of a different postural control strategy (Panzer, Bandinelli & Hallett 1995).

Ekdahl and co-workers have already tested the reliability of the length of the COP sway in standing with the feet together on a sample of 10 healthy subjects tested at 1^{st} and 4^{th} week. The correlation between the length of sway path for weeks 1 and 4 was $r_s=0.80$ ($p<0.01$) indicating good reliability (Ekdahl, Jarnlo & Andersson 1989).

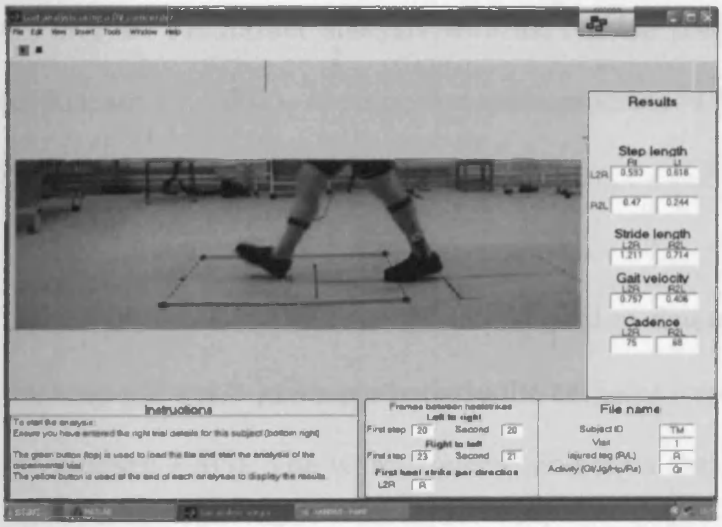
3.10M: Gait Parameters:

Gait characteristics were recorded on two occasions: to measure the spatial and temporal characteristics of walking and to measure the lower extremity joint moments. In both the instances the subjects walked a distance of 12 m at their self-selected pace.

Spatial and temporal parameters of gait were recorded using the Sony digital video camcorder at 25 Hz (Sony digital camcorder, DSR-PD1P, STYLUS, East Tyndall Street, Cardiff, CF24 5EA, UK) during plantar pressure measurement.

Gait was recorded with a digital video camera as the subject walked at a natural speed between the 2 parallel sticks (refer Figure 3.13). Gait velocity, cadence and stride length were calculated using a purpose written programme in Matlab.

Figure 3.13: Gait recording with a digital video camera



The subjects were instructed to walk at their natural pace and three such trials were recorded (refer Figure 3.13). Self-selected gait speed is considered to be the most efficient walking speed for an individual and has been found to be an appropriate predictor of function and disability (Cress et al. 1995, Guralnik et al. 2000). Since the aim of the study was to investigate the functional outcome in terms of daily walking activity it was appropriate to record walking at the self-selected speed. The video clip was downloaded to the computer. The time difference between the 3 consecutive heel strikes was recorded to compute the stride length and stride time. Gait speed was calculated from the stride length and stride time using the Matlab software (van Deursen, Button K & Lawthom C 2001).

The net joint moments during gait were measured using Kistler force platform and 512 Vicon Kinematic systems in RCCK. The preparation of the patient and the equipment remained similar to that adopted for the STS movement analysis (refer Section 4: 3.10K). Subjects were allowed to practice walking over the walkway prior to testing and the data were collected as they walked naturally across the 18m walkway. Three trials were recorded for each subject. The data recorded by the Vicon work station was reconstructed and labelled for further analysis with the Matlab program (The Mathworks, Inc; Version 6.5 Release 13, 2002). A purpose written program in Matlab was used to calculate the net joint moments of the lower limbs.

The technique of inverse dynamics was used to determine the forces and moments at the hip, knee and ankle joints particularly the net joint forces and net joint moments during gait (Vandeursen 2005). The word 'inverse' indicates that the causes of movement i.e. gait in this case (forces and moments) are calculated from the outcome (movement as it is measured).

In addition to the maximum joint moments of the lower extremity, the weight-bearing on both the feet was measured to analyse the symmetry of the walking task. The weight-bearing force on both the sides was measured as the patients walked along the walkway striking one force plate by each foot at a time.

3.10N: Mobility: Self –reported measure:

After completing the performance-based tests, the patients completed the RiverMead Mobility Index (RMI). RMI was used to quantify the patient's perception of their mobility (refer Appendix 4). It comprises questions about 14 activities and direct observation of one activity (Collen et al. 1991). It is a short, simple and clinically relevant tool which concentrates on body mobility covering a range of activities from turning over in the bed to running (Collen et al. 1991).

Three patients were helped to read the items because they forgot their reading glasses. The participants responded to the items as 'YES' or 'NO'. Based on the response, the items were scored 1 (Yes) or 0 (No). The sum of the scores was used to indicate the total score obtained from the RMI. In case of the patients belonging to the TTA group, the items 5 & 10 were scored without considering the use of the lower-limb prosthesis as an "aid" or "support" (Franchignoni, Brunelli, Orlandini, Ferriero & Traballesi 2003).

The instrument has been validated in a variety of neurological diseases (Franchignoni, Brunelli, Orlandini, Ferriero, & Traballesi 2003). It is also reported to be a measure with acceptable levels of internal consistency, construct validity and responsiveness in the assessment of overall body mobility in people with LEA (Franchignoni, Brunelli, Orlandini, Ferriero & Traballesi 2003). Although the tool has not been validated particularly in patients with diabetic peripheral neuropathy, it has been reported to be a valid tool for the assessment of mobility in patients with polyneuropathy (Molenaar, vanDoorn & Vermeulen 1997). Additionally no simple self-reported valid tool was available for this patient group to assess the wide range of mobility tasks better than RMI.

3.10O: Weight-bearing: Plantar Pressure distribution:

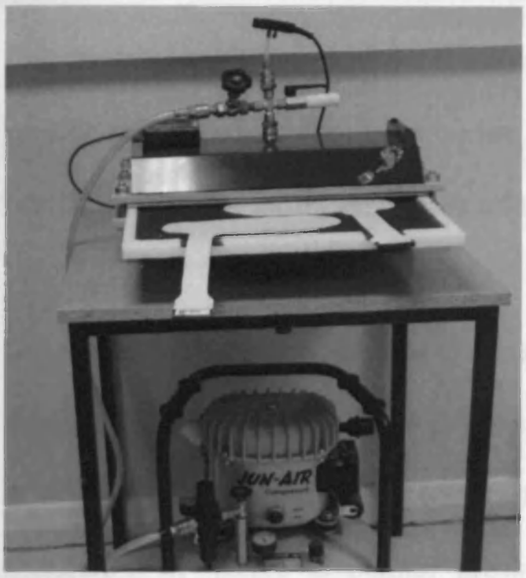
Dynamic plantar pressure distribution during level walking was used to indicate the plantar weight-bearing during walking. Plantar pressures were measured using the Pedar in-shoe pressure measurement system (novel, Gmbh, Munich, Germany) at a sampling rate of 50Hz (refer Figure 3.14).

Figure 3.14: Measurement of plantar pressure using Pedar in-shoe pressure measurement system

All patients were measured in uniform standard footwear (Pullman shoes, Thamert [UK] Ltd, Oxon) with appropriate shoe fillers for the patients with PFA. The respective shoe moulds made from thermocol material were used after wrapping them with stump socks to create a soft interface between the residual foot and the shoe filler. The accurate fitting of the shoe fillers made from the shoe moulds did not allow sliding of the foot within the shoe. Therefore, the plantar pressure distribution was not affected over the partially amputated foot.

Two millimetre thick insoles available in different standard and wide sizes were calibrated using the standard calibration device (novel Gmbh) and the standard calibration procedures with homogenous air pressure ranging from 4 to 60 N/cm^2 (refer Figure 3.15).

Figure 3.15: Calibration of insoles using the standard calibration device (novel Gmbh)



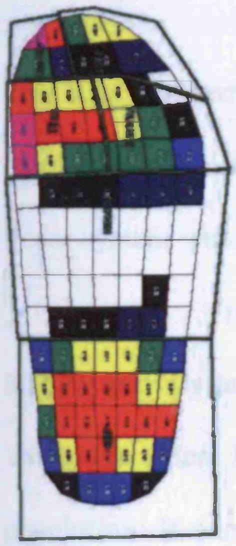
Zero measurement was performed before starting the experimental measurement to ensure a fresh measurement. The procedure was performed for the right and the left foot alternately while the patient stood with the help of a walking frame. Three trials were recorded for each subject (McPoil et al. 1999) as they walked 12m on level ground at their natural pace. The pedar sensor insoles suitable to the size of the patient's feet (sizes- WW.050, XW.112, and VW.115 etc.) were placed inside the shoes and connected to a portable pedar system strapped around the waist of the subject. The data were collected on a handheld iPAQ computer as the patient walked for a distance of 12m. Digital camcorder was used to measure the temporal and spatial characteristics of gait simultaneously (refer to the details of the gait measurement explained in Section 4: 3.10M). The data were then downloaded to the main computer for analysis.

Plantar pressure data were processed and analysed using the novel standard software version 10.33. Five mid-gait steps on the right and left foot were selected for analysis to eliminate the effect of acceleration and deceleration of the gait. The pressure distribution over the total surface area of the foot was measured in addition to the plantar pressures over specific regions of the foot because the MPP over the total surface area of the foot indicates the risk for plantar injury anywhere on the foot.

Individual masks were created for each subject subdividing the foot into six regions namely: heel, midfoot, medial metatarsals (Ist & IInd MT), lateral metatarsals (IIIrd, IVth & Vth MT), hallux and all the toes (refer Figure 3.16). There is a general difficulty in the application of masks to plantar pressure data. Division of the foot on the basis of a geometric algorithm is recommended to standardise result communication and exchange within and between research laboratories (Hennig, 2002). Standardised masks such as PRC mask are available in the novel software (Cavanagh, Rodgers & Iiboshi 1987). However, this study included 4 groups of patients at different stages of foot complications namely: diabetic neuropathy, plantar ulceration, partial foot amputations and trans-tibial amputations resulting in a heterogeneous pool of feet to be studied. The different shapes of the feet resulting from various levels of partial foot amputations made it difficult to apply a standard mask for evaluation of pressure distribution over different feet. Therefore, creation of an individual mask was preferred to application of a standard mask in this study.

Previous studies have created masks based on the regions consistently defined for subjects as a percentage of total length and width of the footprint (McPoil et al. 2001). Based on an extensive literature search and interactive discussions with the Human Movement Scientists working in the field of pressure measurement and the software development team of novel Gmbh (Munich, Germany) the masks were created with the help of visual input from still images. Although this method of mask creation can be criticised to possess the demerit of been subjective it appears to be the best available method to make correct decisions pertaining to the pressure distribution over the feet especially the PFA group.

Figure 3.16: Division of foot into 6 regions (heel, midfoot, medial metatarsals, lateral metatarsals, hallux and toes) using a custom-made mask



Maximum peak pressure (MPP) and Pressure-time integral (PTI) generated by the software were extracted for further analyses. MPP reflects the absolute peak pressure during the gait cycle and was used as a measure of instantaneous peak pressure. Since tissue vulnerability is a factor of both time and pressure (Brand 1983), Pressure-Time Integral (PTI) was studied as the area under the peak pressure-time curve. Daily plantar cumulative stress (DPCS) was calculated as the product of PTI and average daily strides (refer Chapter 2: Literature review; Plantar pressure distribution) obtained from the Step watch Activity Monitor (Maluf & Mueller 2003).

Plantar pressure data obtained from the affected foot of the patients with DFU and PFA were compared to data from the right foot of the control group. Considering the symmetrical pattern of distal polyneuropathy affecting the feet (Guy et al. 1985) data from the right feet of the control group were considered for comparative analysis by default. Prior to considering the data from the right feet for further analysis, the data from the control group was checked that there was no significant difference in the total MPP between the right and left foot in the control group (paired sample t-test, p=0.245).

This measurement system is known to be a valid and reliable system to measure dynamic plantar pressure distribution during walking. The ICC for between trials testing with the Pedar system was 0.99 (McPoil & Cornwall 1995).

3.10P: Activity level: Capacity of walking: Energy Expenditure:

Total Heart Beat Index (THBI) was used as an index of energy expenditure in this patient population. It was used to represent the energy efficiency of gait under non-steady-state conditions.

The two-min walk test was used as a standard exercise to calculate the THBI for all the four groups. One trial of 2 min walk test was used. It is known to be a valid and reliable tool used to assess functional exercise capacity in patients with trans-tibial amputation

(Brooks et al. 2002). The authors had tested for the reliability of this test within a group of subjects with trans-tibial amputations with primary diagnoses as peripheral vascular disease and diabetes.

THBI was computed as a ratio of total number of heart beats to the total distance covered during the exercise (Hood, Granat, Maxwell & Hasler 2002). All the participants were relaxed before the start of the test. The polar heart rate monitor (Polar Electro Oy Fin-90440, Kempele, Finland) was calibrated before the study and programmed to record the heart rate continuously for a two-minute period. They were explained to report any symptoms of exercise intolerance (such as fatigue and shortness of breath) and the test was terminated immediately in the event of any of the symptoms mentioned above. The heart rate sensor was strapped across the chest wall and the monitor which displayed the basal heart rate was held in the hand (Figure 3.17). The patients were instructed to walk for 2 minutes inside the laboratory at a natural pace. The Physiotherapist walked along with the patient to record the distance covered during the two-min walk test using the road measuring wheel (Figure 3.17). The start and end of the 2 min walking period was manually determined by the researcher. The total number of heart beats was extracted from the software which recorded the heart rate continuously for two min. The ratio of the total number of heart beats and the total distance covered during the 2-min walk test was computed to calculate the THBI.

THBI is established to be a valid and reliable tool to provide a measure of energy expenditure in non-steady state conditions (Hood, Granat, Maxwell & Hasler 2002). Repeatability studies in unimpaired subjects and subjects with spinal cord injuries found the THBI to be comparable to oxygen cost and better than the Physiological Cost Index

(PCI). Hood et al. (2002) demonstrated that in unimpaired subjects the THBI had very high reproducibility (ICC=0.950, SDD%=15.7%) for steady-state exercise and high reproducibility (ICC=0.893, SDD%=14.5%) under non-steady state conditions. In their study, the total number of heart beats during the exercise period had an ICC of 0.897 for steady-state exercise and 0.893 for non steady-state exercise (Hood, Granat, Maxwell & Hasler 2002). However, the reliability of this index has not been studied previously in the diabetic population, which is known to present with autonomic neuropathy.

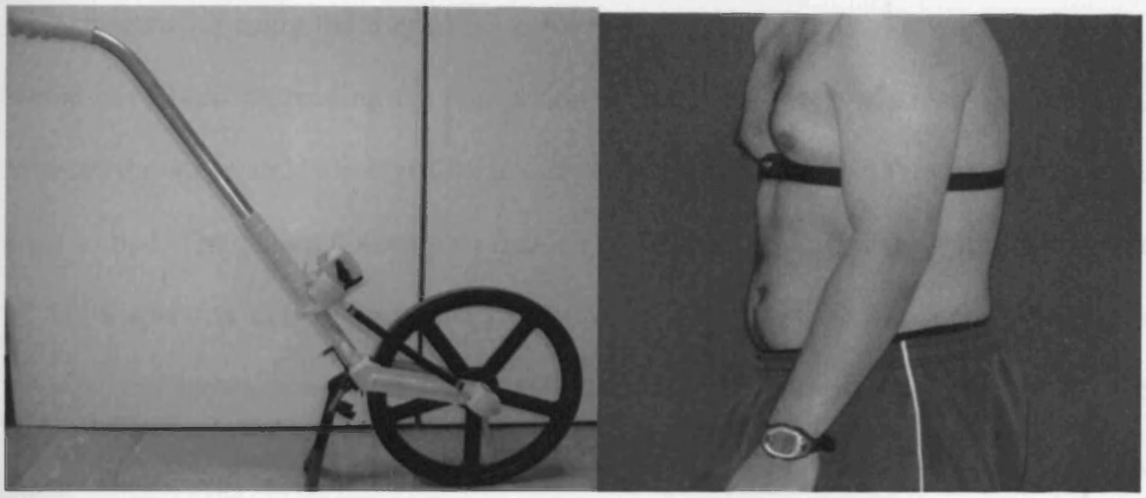
Diabetic autonomic neuropathy is known to coexist with other diabetic complications although it is one of the least recognised. It may be either clinically evident or sub clinical. Considering its major clinical manifestations, namely resting tachycardia, exercise intolerance and orthostatic hypotension, (Vinik et al. 2003) it was necessary to test the reproducibility of THBI in this patient population. Therefore, a reliability study was conducted with 6 patients with DMPN. None of these patients had a history of plantar ulceration. Four patients did not have any history of cardiac or respiratory problems. Whereas 1 patient had a history of myocardial infarction 6 years ago and another patient had a history of hiatus hernia. Both these patients were non-symptomatic at the time of assessment. The patients performed a 2-min walk test, which was repeated three times with a rest period of 10 min in between each trial to return to pre-test heart rate. The total number of heart beats and the distance walked during each trial of 2- min walk test were recorded for the computation of the THBI score.

Reliability of the THBI score was determined using the Intraclass Correlation Coefficient (Fleiss 1999). The ICC was computed as a ratio of total variance as shown in the formula below:

ICC= Var (SUBJECT) / Var (SUBJECT) + Var (Error)

The Var (SUBJECT) and Var (Error) for the THBI score was calculated using SPSS 11. The ICC was 0.96 indicating excellent reliability of the THBI to measure energy expenditure in the diabetic neuropathic population.

Figure 3.17: (Left) - Road measuring wheel & (Right) -Polar heart rate monitor



3.10Q: Activity level: Performance of walking: Average daily walking:

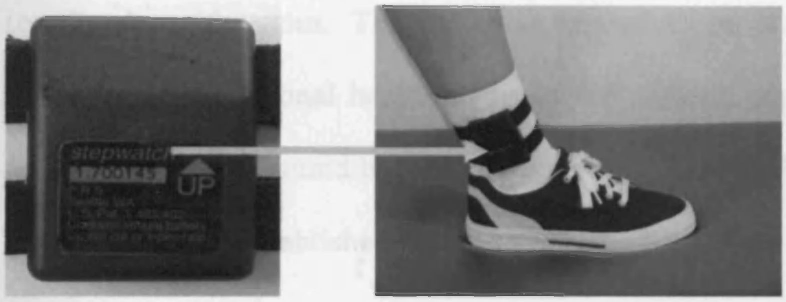
Stepwatch™ Activity Monitors (SAM; Cymatech, Seattle, WA, USA) were used to record the performance of daily walking activity (Shepherd, Toloza, McClung & Schmalzried 1999). The accelerometer-based device measuring 680x50x20 mm was strapped around the subject's right leg laterally above the ankle joint and the monitor was programmed according to the height and gait characteristics of each individual subject (Figure 3.18). In case of patients with TTA on the right side, the monitor was strapped around the prosthetic ankle (Coleman et al. 2004). SAM was tested with a trial of first 40 steps during which the light blinked with each step taken.

The SAM was programmed with an infra-red optical interface prior to monitoring for individual subject settings. Subjects were instructed to wear SAM continuously for eight consecutive days, except when bathing, showering or swimming.

The SAM is designed to measure activity with minimum intrusion in behaviour. The 24-hr record of the number of strides itself was considered as a tool to assess the compliance of the patients with using the Stepwatch activity monitor. Had they not worn the device there would have been no reading for that period. In addition, they were instructed at the outset to wear the stepwatch for eight consecutive days from the time they woke up until they went to bed. The patients were also handed an instruction leaflet regarding the correct use of the Stepwatch activity monitor (refer to Appendix 4) and the accompanying person received the same instructions. They were told to contact the Research Centre for Clinical Kinaesiology in case of any problems with the activity monitor. However, the patients were not asked to maintain a daily log and they were not contacted to ensure they were wearing the stepwatch during the week. The benefit that the stepwatch provides an unobtrusive measurement of walking activity would have been lost if the more intrusive methods were added potentially influencing patient everyday behaviour. The researcher has confirmed that all the data related to daily walking performance from this study sample were complete.

Stepwatch activity monitor records daily walking activity by counting the steps walked per minute for a 24 hr period for the entire measurement period, which can be upto 2 months. SAM is an accelerometer with an inbuilt microprocessor. When the monitor is programmed, it uses the calibration information from the subject settings (height and gait characteristics) for each individual to define a step. The number of strides every one-minute interval were recorded for a continuous twenty-four hours over seven consecutive days. The mean average daily stride count was considered for analysis.

Figure 3.18: The step activity monitor strapped to the right leg above the ankle to record continuous walking for 7 days



The SAM is a reliable and valid tool for the measurement and recording of walking activity (Hartsell, Fitzpatrick, Brand, Frantz & Saltzman 2002).

3.10R: HR-QOL:

SF-36 and Cardiff Wound Impact Scale (CWIS) were used to evaluate the H-RQOL from different but complementary perspectives. A generic measure was selected with the intention of comparing the study population (in this case the diabetic population) with the normal population within similar age groups (Price 2004). In addition, a condition specific-tool was used to investigate the impact of diabetic foot complications on the patient population studied (Price 2004).

All the four groups completed the developmental UK version of SF-36 in its original form (Ware 1993). The questionnaire was read out to 3 patients by the Research Assistant to seek the responses since they had forgotten their reading glasses.

As the primary objective of this study was to explore the functional outcome in the diabetic population with foot complications it was essential to select a tool focussed largely on functional health status. The SF-36 is known to be a reliable and valid tool for the assessment of functional health status in the diabetic population (Jacobson, de Groot & Samson 1994). The sound basis for interpreting SF-36 scales as measures of health and H-R QOL is already established (Ware 1993, Jenkinson et al. 1996).

To explore the relationship between SF-36 scales and general health and quality of life the SF-36 scales were correlated with the General Health scale and with a general measure of quality of life. The results indicated a significant correlation between health status and aspects of quality of life not specifically related to health (Ware 1993, Jenkinson, Layte, Wright & Coulter 1996).

In the present study, the developmental UK version of SF-36 was used to analyse the functional health status (refer to Appendix 4). It measures various domains: Physical functioning, Role functioning, Bodily pain, General health, Vitality, Social functioning, Mental health and Reported Health Transition. It is validated for the population of the UK (Ware 1993, Jenkinson, Layte, Wright & Coulter 1996). Normative data gathered from the healthy population samples of US and UK in different age-groups is available for comparisons (Ware 1993, Jenkinson, Layte, Wright & Coulter 1996).

CWIS: is a valid and reliable condition specific QOL tool developed at the Wound Healing Research Unit in Cardiff (Price & Harding 2004). The tool has undergone extensive piloting to establish its psychometric properties. It gives a profile of score for Well-being, Physical Symptoms and Daily Living and Social life (Price & Harding 2004). Physical Symptoms and Daily Living and Social Life were assessed for both the experience of a given symptom and the associated stress experienced by the individual on a 5-point scale. The domain of Physical symptoms and Daily Living focussed on the impact of symptoms on daily functioning and comfort. The Social Life domain focussed on the individual's ability to get out and about. The domain on Well-being focussed on the patient's Well-Being in relation to the wound, particularly the anxieties about the outcome. Therefore, the domain of Well-Being was assessed only in the DFU group in the present study. All the 3 scales were then transformed onto a 0-100 scale, where a high score indicates a positive rating (Price & Harding 2004).

In addition to the 3 scales CWIS includes, an indication of overall H-R QOL was assessed using a global scale together with an indication of satisfaction with that H-R QOL. The final section of the tool allowed for the collection of relevant information under the sub-heading 'Overall Comments' which may include a note of any significant life events. The scale was modified for use in the study population and corresponding adjustments were made for the scores of the various domains assessed. Cardiff Wound Impact Scale was administered to group DFU in its original form (version-copyright WHRU 1997) whereas the DMPN, PFA and TTA groups completed the questionnaire without the section on 'Well being' since they did not present with active foot ulceration. The domain of Well-Being was therefore not evaluated in the DMPN, PFA and TTA groups. In addition, 6/12 questions pertaining to ulcers were crossed out for the DMPN, PFA and TTA groups and the final score for Physical Symptoms and Daily Living (experience and stress) was modified accordingly. Similarly, 1/7 question pertaining to ulcer was crossed out from the domain of Social Life (experience and stress) for the DMPN, PFA and TTA groups and the final score for Social Life was modified accordingly. Both the original and the modified version of the CWIS are attached to the Appendix 4.

3.11: Summary of outcome Measures:

Appropriate outcome measures were evaluated for each domain of function as presented in the Table 3.5.

Table 3.5: Summary of outcome measures

<table>
<tr><th>Impairment</th><th>Mobility</th><th colspan="2">Activity level</th><th>H-RQOL</th></tr>
<tr><td rowspan="4">Diabetic neuropathy
S-W Monofilaments</td><td>Sit-to-stand
Time taken to complete STS, net joint moments & weight-bearing force</td><td colspan="2" rowspan="2">Walking</td><td rowspan="4">SF-36

Cardiff Wound Impact scale</td></tr>
<tr><td>Standing balance
COP excursion, time to stability</td></tr>
<tr><td>Gait
Gait velocity; stride length; cadence ;
net joint moments & weight-bearing force</td><td rowspan="2">Capacity

Total Heart Beat Index</td><td rowspan="2">Performance

Average daily strides</td></tr>
<tr><td>Plantar weight bearing
Peak Pressure, Pressure Time Integral & Daily Plantar Cumulative Stress</td></tr>
</table>

3.12: Normative data to provide baseline reference to the DMPN group:

Data acquisition:

Normative data from the healthy subjects were extracted from previous studies wherever possible to provide a reference to the findings from the diabetic neuropathic patient groups. Inconsistent methods, use of different equipment and different age groups of patients all make it difficult to compare results between studies. Considering these factors a study as close as possible was selected to provide the reference values from the results.

Standing balance:

Several studies investigating postural stability of healthy subjects were located. Some of which aimed to study the healthy non-diabetic subjects primarily whereas others studied the healthy subjects with the objective of comparing them with the diabetic neuropathic patients.

Yamamoto et al. (2001) included a similar age group (average age 55.7±8.7) as the present study but they used a Gravichart to analyse the static posturography (Yamamoto et al. 2001).

Another study with healthy subjects in a similar age group measured standing balance in terms of the displacement of the COP in the sagittal and lateral directions in addition to the standing time (Hermodsson et al. 1994).

Yet another study tested balance in healthy subjects using a stroop test with the aim of comparing the dual task performance in patients with LEA (Geurts et al. 1991).

Therefore, the most appropriate study to abstract the reference data was the study conducted by Ekdahl et al. (1989) to evaluate the standing balance in healthy subjects (Ekdahl, Jarnlo & Andersson 1989). They included patients with similar age group, conducted 3 trials of the test each for 30 sec using a force platform and used the length of the sway path (cm) to indicate the standing balance. The data from the male subjects (age range 60-64 yr) was extracted as a reference for the current study as the majority of subjects (male=73, female=11) in the present study were males. The test protocol and the equipment were similar to the present study allowing a fair comparison of the results from this study.

Gait:

Several studies have attempted to study the gait pattern in diabetic neuropathic patients in comparison to healthy subjects (Mueller et al. 1994, Courtemanche et al. 1996, Katoulis et al. 1997, Dingwell, Cusumano, Sternad & Cavanagh 2000, Giacomozzi et al. 2002, Sacco & Amadio 2003, Menz, Lord, St George & Fitzpatrick 2004).

Menz et al. (2004) studied gait in healthy subjects in comparison to the diabetic neuropathic patients on level ground and irregular walking surface (Menz, Lord, St George & Fitzpatrick 2004). However, the range of the age group of the healthy subjects was very wide, from 55-91 years making it difficult to compare the findings with the present study (age range, 45-75 yr).

Dingwell et al. (2000) reported the dynamic stability of the patients with DMPN in comparison to age-matched healthy subjects. However, they have not documented the age group of the subjects making it difficult to consider the findings for comparison (Dingwell, Cusumano, Sternad & Cavanagh 2000).

Sacco et al. (2003) studied treadmill gait in patients with DMPN compared to the non-diabetic subjects. Since the features of treadmill gait are different to the level walking, the findings from this study could not be considered either (Sacco & Amadio 2003).
In the first instance the study reported by Mueller et al. (1994) was very close to been suitable to abstract the findings from the healthy subjects (Mueller, Minor, Sahrmann, Schaaf & Strube 1994). They used video analysis technology to assess the gait characteristics. Even the present study used a video technology to record gait parameters but the average age of the healthy subjects was slightly younger (56.8 ±11.3yr) in the study reported by Mueller et al. (1994) compared to the present study.

The most appropriate study appeared to be the one documented by Courtemanche et al. (1996) which studied patients with DMPN in comparison to the healthy subjects on level surface with the age group of the participant very close (60.6±5.6 yr) to the present study (Courtemanche et al. 1996). Therefore, the results from this study were used to provide a reference value for gait velocity.

Energy expenditure (Total Heart Beat Index):

Several studies have reported the measurement of energy expenditure in healthy subjects (Leaf & Macrae 1995, Morio et al. 1997, Hood, Granat, Maxwell & Hasler 2002). However to date only one study has been located which describes the measurement of energy expenditure in healthy subjects using Total Heart Beat Index (THBI) as a measure of energy expenditure (Hood, Granat, Maxwell & Hasler 2002). Therefore, the findings from the same study were used to provide the reference for non-diabetic healthy subjects although the healthy subjects were younger (26.6±6.3) compared to the diabetic patients of the present study. The fact that the healthy subjects were younger compared to the diabetic patients has been considered in the interpretation of the results from the THBI score.

Daily walking performance:

Although there are several studies which have documented the average daily walking, (Shepherd, Toloza, McClung & Schmalzried 1999, Hartsell, Fitzpatrick, Brand, Frantz & Saltzman 2002, Silva et al. 2002, Tudor-Locke, Bell, Myers, Harris, Lauzon & Rodger 2002) Busse (2004) has used exactly the same method and equipment to report the average daily walking based on a 24-hr continuous unobtrusive monitoring for a 7-day period with a step-activity monitor in healthy subjects with an average age of 60.7 years. Therefore, the findings from this study were used as a reference value for healthy subjects. Moreover, the sample of the subjects belonged to the same geographical area as the diabetic patients and therefore any likely effect of the geographical area on the daily walking performance was ruled out making the data even more valid for comparison.

Range of motion (ROM):

Several textbooks report the normal range of motion for healthy subjects for various joints of the lower extremity. However, the ROM reported by Roach & Miles (1991) was the most appropriate because of the similar age group studied. Based on the data from 523 subjects measured with goniometry in the supine position (similar testing position for hip and knee flexion as described in the present study) the authors reported an average of 131 deg of knee flexion and 118 deg of hip flexion (with the knee flexed) (Roach & Miles 1991). The normative data for the ankle joint and the 1st MTP joint extracted from the textbooks are presented in Table 3.6.

Health-related Quality of Life (H-RQOL):

The normative data were extracted from the population norms in the British context provided by the Oxford Healthy Life Survey 1991/2, Health Services Research Unit, Oxford (Jenkinson et al. 1996). The mean scores for Physical Functioning and Social Functioning from 525 subjects with age group (60-64 yr) closest to that of the present study (62.8 yr) were 76.2 and 86.2.

The normative data from healthy subjects for the various outcome measures is summarised in Table 3.6.

Table 3.6: Normative data from healthy subjects

Outcome measure	Mean (S.D.)	Reference
COP excursion (m)	0.551 (0.172)	Ekdahl et al. 1989
Gait velocity (m/sec)	1.32	Courtemanche et al. 1996
THBI (beats/m)	1.24 (0.18)	Hood et al. 2002
Average daily strides	6388 (1563)	Busse 2004
ROM: Hip flexion	118°	Roach & Miles 1991
ROM: Knee flexion (with thigh flexed)	131°	Roach & Miles 1991
ROM: Ankle Dorsiflexion-Plantarflexion	Dorsiflexion: 0-20° Plantarflexion: 0-50°	Brown & Yavarsky 1987
ROM: 1st MTP flexion-extension	Flexion: 0-50° to 0-60° Extension: 0-30° to 0-40°	Kapandji 1987
SF-36 (Physical Function)	76.2 (22.3)	(Jenkinson et al.1996)
SF-36 (Social Function)	86.2 (22.7)	(Jenkinson et al.1996)

3.13: Statistical methods:

3.13A: Statistical analysis for hypothesis testing:

The 4 groups namely DMPN, DFU, PFA and TTA were compared based on their functional outcome. Minimum sample size was calculated using a standardised difference of 1, a power of 0.8 (α= 0.05). Each group needed a minimum of 23 participants. Gait parameters especially gait velocity is known to be a measure of functional performance (Potter, Evans, & Duncan 1995). Moreover, the data for gait parameters was available in the published literature for power calculation. Therefore based on a number of gait parameters reported by Mueller et al. (1994) a range was found for the standardised difference between 1.15 and 1.57 (Mueller, Minor, Sahrmann, Schaaf & Strube 1994). For this power calculation, a conservative estimate of the standard difference of 1 was used.

The total numbers of patients studied in the four groups were as follows: Group DMPN n=30, Group DFU n=23, Group PFA n= 16 & Group TTA n=22. Reasons for inadequate number of subjects with unilateral healed PFA are explained earlier (Chapter 3: Section 3). The challenge to recruit adequate numbers in this group had an impact on the statistical analysis of the results. Two-to-one (Controls: PFA) matching of subjects appeared to be an appropriate strategy in such a case.

The approach to statistical analyses was as follows (refer Figure 3.19):
SPSS 11.0 software was used for statistical analyses of the data (SPSS Inc.). Continuous data were assessed for normality and equality of variances. Normal distribution was tested using Q-Q plots. Kolmogorov- Smirnov test was conducted to confirm the normality (Armitage, Berry & Matthews 2002) whenever required. The four groups were matched on marginal distributions for age, height, body mass and body mass index as these variables

would potentially affect the findings from the biomechanical variables (Bland & Altman 1994). Therefore, an overall one-way ANOVA was conducted to confirm that there were no statistically significant differences in the four variables between the four groups. All the remaining patient characteristics were analysed descriptively without performing inferential statistical tests, as the present study was not designed to test those hypotheses. Primary analyses included comparison of all the four groups and correlation testing for specific confounding factors. An overall One- way ANOVA was used to investigate the differences between the four groups (Altman & Bland 1996). Linear polynomial contrast was used to examine the differences more closely to see what pattern emerges (Armitage, Berry & Matthews 2002). The investigation was structured to examine whether the results from the various outcome measures indicated a decline in function across the four groups.

In the event of significant differences between the groups post-hoc analyses for multiple comparisons to investigate where the difference lay between the four groups were considered. However, the decision to perform multiple testing was confounded by the dilemma of conducting novel investigations in a minimally explored area of interest (e.g. specific performance of patient groups with DFU, PFA and TTA) on one hand whereas on the other hand there was a danger of data dredging.

Therefore, a reasonable approach was adopted to investigate the differences between the DFU, PFA and TTA groups for reasons discussed earlier. Two separate comparisons were performed in the secondary analyses of the data. Independent sample t-test was used to compare the DFU vs. PFA groups and the PFA vs. TTA groups. As a result of multiple testing standard Bonferroni procedure was used to correct the significance level (Armitage, Berry & Matthews 2002) when appropriate.

The potential influence of the likely confounding factors on certain outcome measures was examined using the appropriate tests for Correlation described in the respective section of the Results chapter.

Reliability of the THBI score was determined using the Intraclass Correlation Coefficient (Fleiss 1999). ICC was computed as a ratio of total variance as shown in the formula below:

ICC= Var (SUBJECT) / Var (SUBJECT) + Var (Error)

The Var (SUBJECT) and Var (Error) for the THBI score was calculated using SPSS11.

Summary statistics were presented as group mean and standard deviation (S.D.) / median and interquartile range (IQR). Interactive bar graphs were used to plot the group means ± S.E. / medians for visual comparison of the data.

Figure 3.19: Approach to statistical analyses for hypothesis testing

Primary analyses

Comparison of all the 4 groups

[One-way ANOVA/ One-way analysis of co-variance]

↓ Non-significant difference ↓ *No further analysis was conducted*

↓ Significant difference ↓ Linear polynomial contrast

Secondary analyses

Comparison of specific groups

Comparison of DFU vs. PFA	**Comparison of PFA vs. TTA**
Independent sample t- test	Independent sample t- test
Bonferroni correction	Bonferroni correction

3.13B: Exploratory statistics:

After performing the statistical analyses required for the hypothesis, testing of the study it was interesting to explore the associations between the three domains of function. The fundamental objective of the study was to analyse how patients at different stages of foot complications perform in various domains of function. A multi-dimensional comprehensive model of function was used with the objective of evaluating function in various domains. Further to this information, it was interesting to explore the relationship between the 3 domains of function. Although it was speculated that the three domains might be inter-related it was unclear as to how they link with each other. Therefore it was decided to explore the association between the domains namely mobility, activity and H-RQOL.

Secondly, although the comprehensive nature of the proposed model ensures complete assessment of function in the presence of foot complications, implementation of such a model in clinical practice demands elaborate time, resources and expertise. Availability of all the three cannot be guranteed in an environment of limited resources for cost-effective care. However, the fact cannot be overlooked that clinical practice needs a feasible option to grade the functional outcome and monitor the effect of rehabilitation over time. Therefore three outcome measures representative of each domain were selected for analysis. The choice of the appropriate parameter within each domain is discussed below.

In the patient population at risk of plantar injury due to DMPN, the common weight-bearing mobility task of daily living i.e. walking was thought to be most appropriate to represent the mobility domain. Gait velocity being the most suitable indicator of the gait characteristic (Andriacchi, Ogle & Galante 1977) was chosen to describe the feature of the gait. Moreover, it is identified that all measurements of gait (spatial, temporal, kinematic and kinetic) depend on walking speed (Simoneau 2002). It was believed that the gait velocity may have direct reflection on the performance of walking activity rather than the capacity of walking as gait velocity has been used in the past to indicate the level of function in elderly people (Potter, Evans & Duncan 1995). Moreover, the gait velocity is the simple clinical measure compared to the analysis of STS transfer and standing balance.

However, before making the choice of gait velocity as the most appropriate measure to represent the domain of mobility, the association between the parameters within the domain of mobility were assessed. The time taken to complete the STS transfer i.e. the time taken for full extension during the STS transfer was considered as the parameter equivalent to gait velocity which indicated the time taken to walk a defined distance. Therefore, the association between time to full extension and gait velocity was tested to assess the association between STS transfer and gait. It was thought that the ability to perform a mobility task in the upright posture would be associated with the balance in that posture and therefore the relation between gait velocity and the COP excursion during quiet standing was tested.

Additionally the association between impairment and the task of mobility was assessed by testing the correlation between the lower limb muscle strength and gait velocity. It is established that while walking during the loading phase the hip extensors and knee extensors work to prevent the collapse of the lower limb caused by the line of action of the ground reaction forces located behind the hip and knee joint (Simoneau 2002). The ankle plantar flexors are known to generate power, which is responsible for a large portion of the propulsive forces pushing the body forward during gait (Kepple, Siegel & Stanhope 1997). Additionally, it is established that the hip and knee joints extend along with plantar flexion of the ankle from seat-off to the end of the movement to control the direction of GRF (after seat-off the GRF points in front of the hip and ankle joint and passes far behind the knee) necessary to maintain the postural balance (Roebroeck et al. 1994). Therefore, the strength of hip extensors, knee extensors and ankle plantar flexors was considered most crucial during walking and STS transfer and their relation with the performance of gait was analysed to test the association between impairment and mobility in these patients with foot complications.

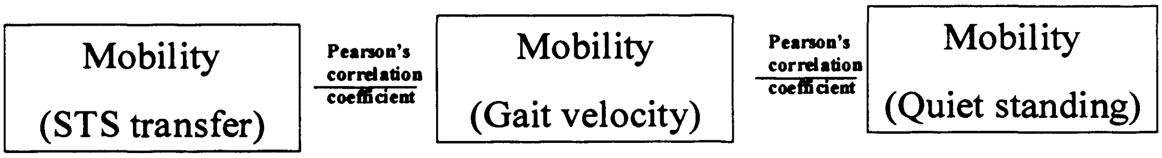
Average daily walking being a direct measure of the performance of walking activity was chosen to reflect the domain of activity and indicated the level of plantar cumulative stress in these individuals. To test the contention that capacity and performance of walking may be associated with each other the association between the THBI score and average daily strides was examined.

It was speculated that the performance of walking might have an association with the patients own perception of the aspect of physical function of their H-RQOL. Therefore physical function as scored by SF-36 was used as the subset indicator of H-RQOL to examine the association between the level of walking activity and H-RQOL.

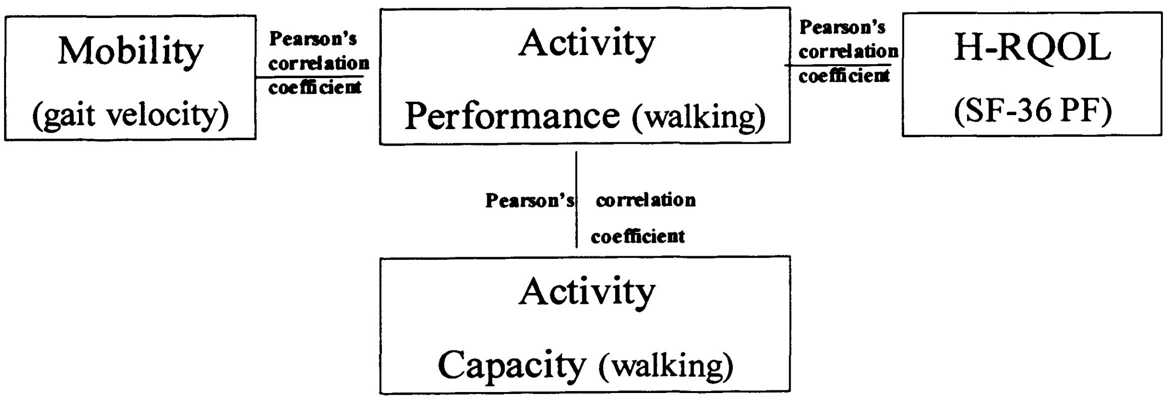
The statistical analyses were purely exploratory rather than being driven by hypothesis testing. Pearson's correlation coefficient was used to examine the association between the domains of function namely mobility, activity and H-RQOL (Munro 1997). The descriptors attached to the strength of the correlation are as follows: 0.00-0.25=little if any, 0.26-0.49=low, 0.50-0.69=moderate, 0.70-0.89=high, 0.90-1.00=very high (Munro 1997). The outcome measures selected for analyses are presented in Figure 3.20. Part A of the figure demonstrates the analysis within the domain of mobility, whereas part B demonstrates the analysis between the 3 domains of function.

Figure 3.20: Approach to statistical analyses for exploratory analyses

Part A: Analysis within the domain of mobility



Part B: Analysis between the 3 domains of function



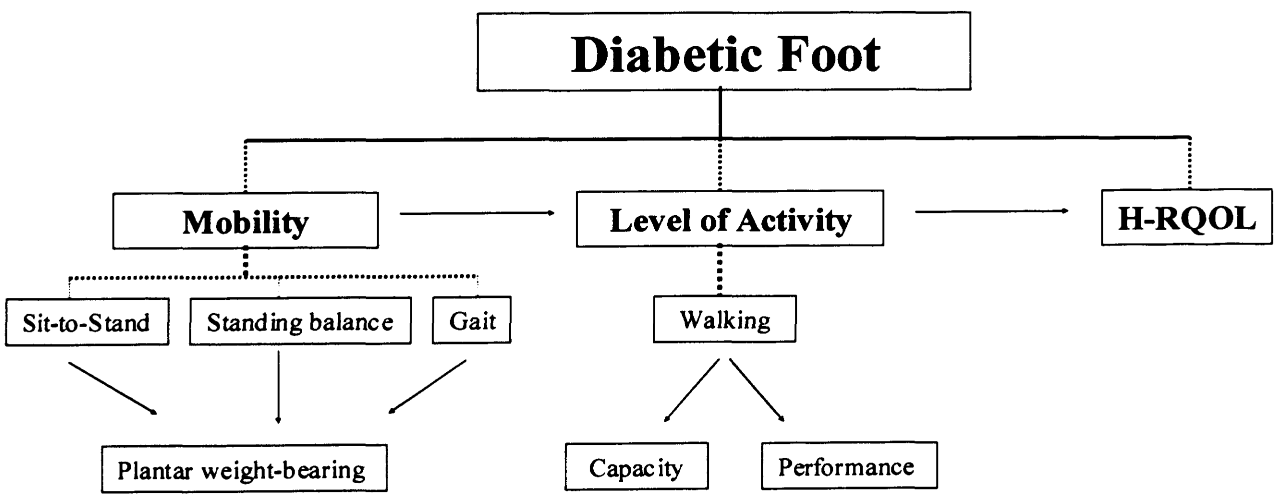
Chapter 4: Results

This chapter is divided into two sections. Section 1 presents the results related to the hypothesis testing and Section 2 presents the results related to the exploratory analysis.

The Section 1 is further divided into two sub sections. The subject characteristics of all the 4 groups are outlined in Sub section 1 and the results of the various outcome measures of function are presented in Sub section 2.

The Sub section 2 is further classified as Part I: Primary analyses and Part II: Secondary analyses. Primary analysis involves the comparison of all the 4 groups and investigation of the trend across the groups wherever applicable. Secondary analysis involves specific group comparisons between the DFU, PFA and TTA groups. The DFU and PFA groups are compared and then the PFA and TTA groups are compared. Sub section 2 reports the results in the order that follows the structure of the model of foot function described previously (Figure 4.1).

Figure 4.1: Proposed model of functional outcome



Section 1: Results from Hypotheses testing

Sub section 1: Results from the subject characteristics

The four groups were matched on marginal distributions for age, height, body mass and BMI. Table 4.1 presents the demographic features of the subjects belonging to the 4 groups. The standard deviations of the demographic features of the 4 groups were fairly similar allowing matching on marginal distributions. However, between the 4 groups the DMPN group appeared to have the smaller deviations compared to the remaining 3 groups. Such an observation suggested that the DMPN patients with further foot complications such as DFU, PFA and TTA appeared to present with relatively larger variation in their demographic characteristics within the respective groups.

Table 4.1: Demographic variables of the subjects presenting group means and standard deviations (SD) along with group comparisons for appropriate variables

Subject characteristics	Group DMPN (n=23) Mean (SD)	Group DFU (n=23) Mean (SD)	Group PFA (n=16) Mean (SD)	Group TTA (n=22) Mean (SD)	ANOVA
Age (yr)	65.48 (4.34)	60.70 (9.31)	62.13 (8.83)	62.86 (6.08)	$F_{3,83}$=1.712 p=0.171
Height (cm)	174.69 (8.27)	177.60 (9.12)	175.54 (8.73)	174.14 (5.34)	$F_{3,83}$=0.828 p=0.482
Body mass (kg)	93.22 (11.95)	97.63 (18.42)	93.98 (18.90)	95.45 (14.65)	$F_{3,83}$=0.327 p=0.806
BMI (kg/m2)	30.56 (3.48)	30.91 (5.55)	30.50 (6.12)	31.42 (4.21)	$F_{3,83}$=0.156 p=0.925
Gender (F/M) Frequency	4/19	4/19	1/15	2/20	N/A

However, one-way ANOVA did not reveal differences among the group means of age, height, body mass and Body Mass Index (BMI). Although the frequency distribution based on gender indicated a higher proportion of men in all the four groups.

The information related to duration and type of diabetes is presented in Table 4.2.

The DFU, PFA and TTA groups consistently showed a greater number of patients with Type 2 DM compared to Type 1 DM. The DMPN group however showed a greater number of patients with Type 1 DM compared to Type 2 DM.

The DMPN group presented with least duration of DM whereas the PFA group presented with the longest duration of DM. The DFU and the TTA groups were very similar in their time duration.

Table 4.2: Diabetes related information

Diabetes information	Grp DMPN	Grp DFU	Grp PFA	Grp TTA
Type of DM (I/II) Freq	13/10	4/19	7/9	6/16
Duration of DM (yr) Mean (S.D.)	10.7 (9)	18.5 (11.6)	20.4 (13.2)	18.2 (11)

The general health related information and family structure of the patients are presented in Table 4.3. The Frequency of patients who smoked, presented with history of cardiac disorders, history of respiratory disorders and the proportion of patients who lived alone vs. patients who lived with family or carer are presented. None of the patients presented with acute clinical manifestations of cardiac or respiratory disorders. Patients with history of cardiac and respiratory disorders were clinically stable at the time of assessment.

Table 4.3: General health related information and family structure

Variables	DMPN (n=23)	DFU (n=23)	PFA (n=16)	TTA (n=22)
Smoking (No. of subjects)	2	5	3	2
Hypertension (No. of subjects)	13	10	5	10
H/o cardiac disorders (No. of subjects)	5	8	1	5
H/o respiratory disorders (No. of subjects)	1	1	0	4
Family structure (No. of patients lived alone/No. of patients lived with family or carer)	3/20	4/19	2/14	4/18

The location of plantar ulceration among the patients of the DFU group is presented in Table 4.4. The wound dressings were not removed during the assessment session. Specific information pertaining to the wounds was extracted from the medical records. The dimensions of the wounds are detailed in Table A3.2 in Appendix 3. The DFU group had a mixture of ulcers; with a majority of patients with fore-foot ulceration (n=18) compared to the heel (n=5).

Table 4.4: Location of plantar ulceration among the patients of DFU group

Site of plantar ulceration	No. of subjects (n=23)
Toe	3
MTP 1-2	7
MTP 3-5	6
Hallux	2
Heel	5

Foot amputation such as hallux, hallux with toes, ray and trans-metatarsal amputations were collectively classified as PFA for this study. The various types of PFA are detailed in Table 4.5. Out of the 5 patients with ray amputations, 3 patients had 1st ray amputation, 1 patient had 2nd ray amputation and 1 patient had complete 1st ray and partial 2nd ray amputation. Out of the two patients who had amputations of the hallux and the toes, one patient had amputation of hallux and second-third-fifth toes. The other patient had an amputation of hallux and second toe.

Table 4.5: Types of Partial Foot Amputations

Type of PFA	No. of patients (n=16)
Hallux	4
Hallux+toes	2
Ray	5
Trans-metatarsal	5

All the patients with TTA had unilateral healed amputation. All the TTA group patients were capable of walking independently to perform their activities of daily life with or without a walking aid. However, no walking aids were used during the testing procedures. The patients with TTA always used their artificial limb for walking. The Artificial Limb and Appliance Centres had used a total surface bearing socket for the prosthesis wherever possible. All the subjects with TTA had completed at least six months following rehabilitation at the time of discharge from Artificial Limb and Appliance Centres (South Wales).

Sub section 2: Results from the outcome measures:

The data from the various outcome measures were tested for normal distribution. Based on visual inspection of the Q-Q plots, wherever the plots appeared skewed, the Kolmogorov-Smirnov (K-S) test was conducted to investigate the distribution (refer to Appendix 3). The K-S test was conducted in combination with exploration of the significance results from the equivalent non-parametric test namely Kruskal-Wallis (K-W). Since the significance results from the K-W test matched with significance results from the ANOVA (except in case of one variable i.e. MPP over the midfoot region of the affected foot wherein the ANOVA revealed significant result i.e. p=0.007 and the K-W test revealed non-significant result i.e.p=0.241. Please refer to the results from the MPP on page 167) further analyses and interpretation of the findings was proceeded based on the results from the ANOVA.

Additionally, since the data from the various variables demonstrated a wide range of variance, equality of variance was not assumed for all the data. Therefore, the corresponding significance values for the parametric tests were considered to report the significance level. Overall, no major departures from the necessary parametric assumptions were evident.

The group means and standard deviations are presented in the tables along with the respective significance values. The sequence of the results follows the structure of the model of function.

4.1: Impairment:

4.1A: Diabetic neuropathy

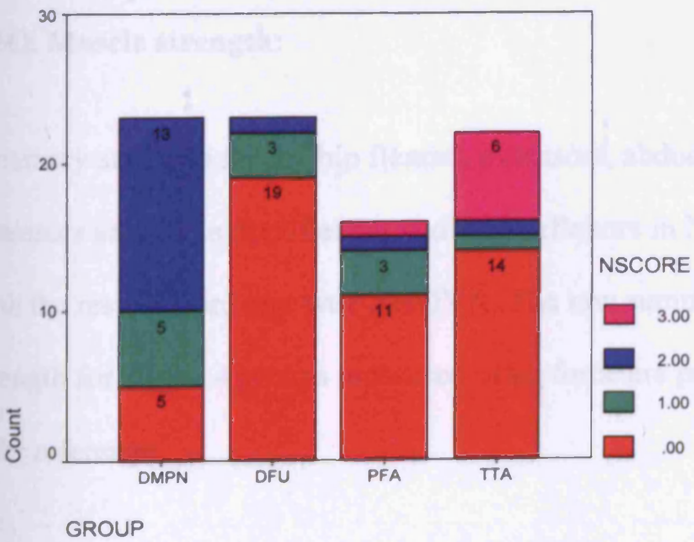
The primary inclusion criterion for all the participants in the 4 groups was DMPN. Table 4.6 presents the neuropathy score for all the participants. Zero (0) was the lowest score whereas 3 were the maximum score. Kruskal-Wallis test was used to compare the score between the 4 groups.

Table 4.6: Neuropathy score measured by S-W monofilaments

Score Min=0; Max=3	DMPN (n=23)	DFU (n=23)	PFA (n=16)	TTA (n=22)	Significance Kruskal-Wallis
0	5	19	11	14	Chi-square= 17.619_3 p=0.001*
1	5	3	3	1	
2	13	1	1	1	
3	-	-	1	6	

The score was significantly different between the 4 groups (p=0.001). The DFU group demonstrated severe loss of sensations (in terms of the number of people with complete sensory loss) followed by the PFA group and then the TTA group (refer Figure 4.2).

Figure 4.2: Neuropathy score (0, 1, 2, 3) among the 4 groups



4.1B: Vibration sensation:

The following results (Table 4.7) show that 64.3% of patients with DMPN confirmed with loss of protective sensation detected by 5.07 S-W monofilament showed loss of vibration perception, whereas 34.5% of patients with loss of protective sensation detected by 5.07 S-W monofilament showed intact vibration perception.

Table 4.7: Results from the vibration perception testing for all the 4 groups.

Score 0 indicates loss of vibration perception whereas 1 indicates vibration perception intact.

Vibration sense at 1st MTP	DMPN	DFU	PFA	TTA	Kruskal Wallis
Score (0/1) (no of patients)	10/12	18/5	11/5	15/7	Chi square=5.605 df=3 p=0.132
Median (IQR)	1 (0-1)	0 (0-0)	0 (0-1)	0	

4.1C: Muscle strength:

Summary statistics for the hip flexors, extensors, abductors, adductors, knee flexors and extensors and ankle dorsiflexors and plantarflexors in N.m are presented in Table 4.8 along with the results from one-way ANOVA. The raw summary data of the lower limb muscle strength for all the 4 groups measured in kg force are presented in Table A3.1 in Appendix 3 for reference.

Comparison of the average scores of the muscles around the hip (flexors, extensors, abductors and adductors), knee (flexors and extensors) and ankle (dorsiflexors and plantar flexors) indicates that there was fairly equal dispersion of the hip muscle strength scores between the four groups. The knee flexors (p=0.013) and extensors (p=0.039) on the affected limb were significantly different between the four groups with the TTA group demonstrating the least average group scores. The ankle dorsiflexors (p=0.028) and plantar flexors (p=0.039) on the contra-lateral limb varied significantly between the 4 groups with the TTA group demonstrating the least average group scores.

Table 4.8: Score for muscle strength in N.m for all the 4 groups

Muscle strength (N.m)	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	ANOVA $F_{df,n}$
Hip flexors (affected)	58.6 (25.2)	62.9 (26.3)	56.9 (21.2)	54.2 (21.5)	0.478_3=0.699
Hip flexors (contra-lateral)	54.0 (23.4)	65.5 (25.9)	55.58 (21.1)	49.2 (16.7)	1.980_3=0.124
Hip extensors (affected)	61.0 (27.3)	68.5 (25.9)	60.4 (27.1)	60.7 (20.1)	0.481_3=0.697
Hip extensors (contra-lateral)	60.5 (29.0)	69.8 (24.9)	62.8 (24.4)	53.2 (18.9)	1.560_3=0.206
Hip abductors (affected)	54.6 (23.7)	55.8 (23.1)	55.9 (21.4)	51.4 (16.3)	0.186_3=0.905
Hip abductors (contra-lateral)	53.0 (22.9)	56.2 (21.8)	55.9 (18.1)	49.9 (15.8)	0.424_3=0.737
Hip adductors (affected)	63.6 (27.0)	65.8 (24.9)	60.8 (22.7)	59.8 (20.4)	0.259_3=0.855
Hip adductors (contra-lateral)	58.2 (26.6)	70.3 (26.5)	64.6 (24.9)	53.5 (17.2)	1.878_3=0.140
Knee flexors (affected)	28.9 (12.9)	33.2 (15.0)	28.1 (10.3)	20.9 (8.9)	3.843_3=0.013*
Knee flexors (contra-lateral)	28.9 (12.9)	35.6 (17.9)	27.3 (8.7)	29.3 (11.7)	1.470_3=0.229
Knee extensors (affected)	54.2 (22.7)	55.9 (26.4)	52.6 (18.6)	38.7 (16.7)	2.917_3=0.039*
Knee extensors (contra-lateral)	50.3 (21.7)	57.4 (23.3)	59.8 (26.1)	44.6 (12.9)	2.102_3=0.107
Ankle plantarflexors (affected)	17.9 (7.7)	n/a	13.3 8.1	n/a	2.571_1=0.119
Ankle plantarflexors (contra-lateral)	16.9 (7.2)	19.1 (7.9)	14.9 (9.3)	12.4 (6.4)	2.935_3=0.039*
Ankle dorsiflexors (affected)	13.9 (6.0)	n/a	13.3 (6.9)	n/a	0.047_1=0.830
Ankle dorsiflexors (contra-lateral)	14.0 (5.2)	15.0 (5.4)	13.6 (5.4)	10.7 (2.7)	3.204_3=0.028*

4.1D: Foot deformities:

The descriptive statistics for the dispersion of the deformities of the feet of the patients of the 4 groups are presented in the Table 4.9. It was observed that the foot deformities had a bilateral presentation in the DMPN and the DFU groups. None of the patients presented with total obliteration of the medial longitudinal arch of the foot or Charcot arthropathy. Presence of acute symptoms of Charcot arthropathy was defined as a criterion to exclude patients from the present study. Three patients with active Charcot arthropathy were excluded from the disease because their feet were protected in total contact cast and the patients were instructed to adhere to complete non-weightbearing on the affected foot. The common deformities noted were hallux valgus, claw toes, cavus foot and a combination of hallux valgus with claw toes. The dispersion of the foot deformities across the 4 groups appeared to be similar in the 4 patient groups.

Table 4.9: Dispersion of foot deformities across the 4 groups

Foot deformity	DMPN (n)	DFU (n)	PFA (n)	TTA (n)
Hallux valgus	4	3	3	3
Claw toes	4	4	4	5
Cavus foot	0	1	0	1
Hallux Valgus+Claw Toes	0	2	0	0

4.1E: Joint motion:

The summary statistics for the hip, knee and ankle joint motion in the sagittal plane are expressed in degrees for all 4 groups.

Table 4.10: Hip, knee and ankle joint motion in the sagittal plane (expressed in degree) for all the 4 groups

Joint ROM (degree)	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	ANOVA $F_{df,n}$
Hip (sagittal) (affected)	98 (11)	101 (18)	103 (12)	99 (8)	0.567_3 p=0.639
Hip (sagittal) (contra-lateral)	96 (10)	96 (17)	103 (10)	97 (7)	1.313_3 p=0.276
Knee (sagittal) (affected)	130 (7)	132 (9)	130 (13)	131 (8)	0.294_3 p=0.830
Knee (sagittal) (contra-lateral)	131 (7)	133 (9)	131 (14)	130 (9)	0.370_3 p=0.775
Ankle (sagittal) (affected)	36 (14)	38 (12)	30 (10)	-	1.710_2 p=0.190
Ankle (sagittal) (contra-lateral)	41 (16)	38 (10)	31 (14)	33 (9)	2.670_3 p=0.053
1st MTP (sagittal) (affected)	69 (19)	29 (13)	-	-	65.702_1 p<0.001*
1st MTP (sagittal) (contra-lateral)	68 (22)	36 (16)	41 (19)	45 (25)	9.734_3 p<0.001*

The results from one-way ANOVA demonstrate significant difference in the 1st MTP joint motion (refer Table 4.10) on the affected foot (p<0.001) and the contralateral foot between the groups (p<0.001). On the affected side, the MTP joint motion was compared only between the DMPN and DFU group as the data was not available for the PFA and TTA groups for obvious reasons.

4.2: Mobility:

4.2A: Sit-to-stand:

Table 4.11 presents the group means along with the standard deviations of the time taken to complete the full extension, which indicated the completion of the STS task, and the time taken to attain stability following full extension, which indicated dynamic stability during the task. There was no significant difference between the 4 groups in the time taken to attain full extension and the time taken to stabilise after full extension (refer Table 4.11).

Table 4.11: Group means and standard deviations for Time to stability and Full extension for the 4 groups

	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	ANOVA $F_{df,n}$
Full extension (s)	1.5 (0.3)	1.6 (0.5)	1.6 (0.3)	1.9 (1.4)	$F_{3,83}$=1.546 p=0. 209
Time to stability (s)	6.8 (3.7)	9.1 (3.6)	7.4 (3.9)	7.5 (3.3)	$F_{3,77}$=1.584 p=0.201

Net joint moments:

Primary analysis: Table 4.12 presents the group means along with the standard deviations of the net joint moments (N.m) of the ankle, knee and hip on both the sides during STS movement. The means of the 4 groups were compared using One- way ANOVA. The F-values are presented with the corresponding degrees of freedom (df) and the total number of patients (n). A linear polynomial contrast was used to investigate the trend across the four groups.

Table 4.12: Comparison of net joint moments of the ankle, knee and hip during sit-to-stand movement

Primary analyses							**Secondary analyses**	
STS Joint moments (N.m)	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast C.I. p value**	**DFU vs PFA t_{df} p value**	**PFA vs TTA t_{df} p value**
Ankle (affected)	45.9 (26.6)	43.3 (18.4)	41.0 (13.0)	30.2 (20.6)	$F_{3,82}$=2.415 p=0.073	N.A.	N.A.	N.A.
Ankle (contra-lateral)	37.6 (9.2)	51.0 (17.7)	44.0 (10.7)	56.7 (19.6)	$F_{3,82}$=6.631 p<0.001*	4.817 – 17.695 p=0.001*	1.509 $_{35.078}$ p=0.140	-2.551 $_{33.850}$ p=0.015*
Knee (affected)	42.0 (18.2)	44.8 (20.2)	46.2 (16.8)	29.6 (16.5)	$F_{3,82}$=3.650 p=0.016*	-15.681 – -0.365 p=0.040*	-0.235 $_{35.298}$ p=0.816	3.029 $_{32.118}$ p=0.005*
Knee (contra-lateral)	45.4 (13.7)	46.9 (20.1)	46.5 (22.9)	52.4 (17.1)	$F_{3,82}$=0.631 p=0.597	N.A.	N.A.	N.A.
Hip (affected)	61.7 (20.2)	69.1 (24.7)	68.2 (28.7)	46.5 (20.3)	$F_{3,82}$=4.269 p=0.008*	-20.318- -0.552 p=0.039*	0.101 $_{29.457}$ p=0.920	2.597 $_{25.536}$ p=0.015*
Hip (contra-lateral)	57.2 (21.8)	72.6 (22.6)	62.5 (25.9)	86.3 (30.1)	$F_{3,82}$=5.582 p=0.002*	6.564- 27.977 p=0.002*	1.246 $_{29.675}$ p=0.222	-2.610 $_{34.843}$ p=0.013*

N.A.: Not Applicable **Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.**

On the affected side the four groups showed significant differences in the net joint moments of the knee (p=0.016) and the hip (p=0.008). Significant linear polynomial contrasts indicate a decline in the net ankle, knee and hip joint moments from DMPN to TTA groups (refer Table 4.12). Although the 4 groups do not demonstrate a consistent decline in the net joint moments it is clear that the knee and the hip moments were least on the amputated side in the TTA group resulting in a significant linear contrast (refer Figure 4.3 and 4.4 respectively).

Figure 4.3: Mean values of the net knee moments (N.m) on the affected side during STS (stskma) for the four groups. The error bars present the mean +/- 1.0 S.D.

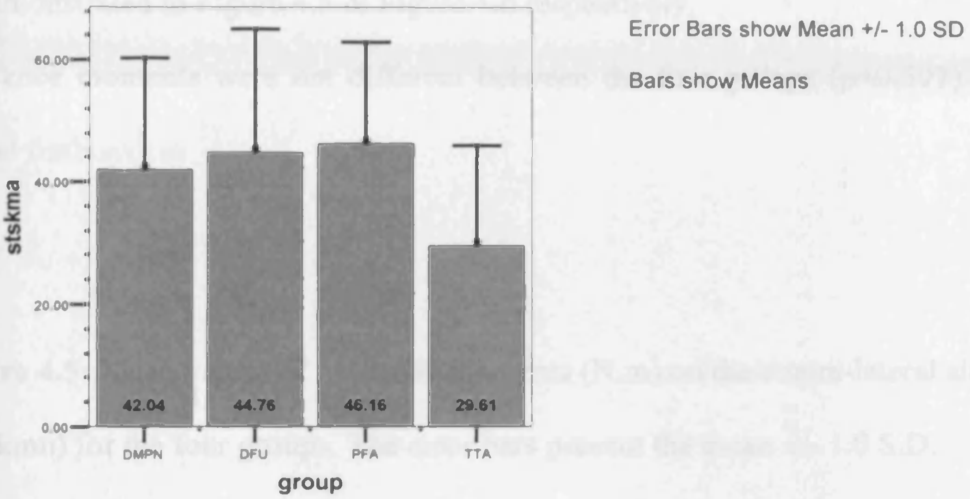
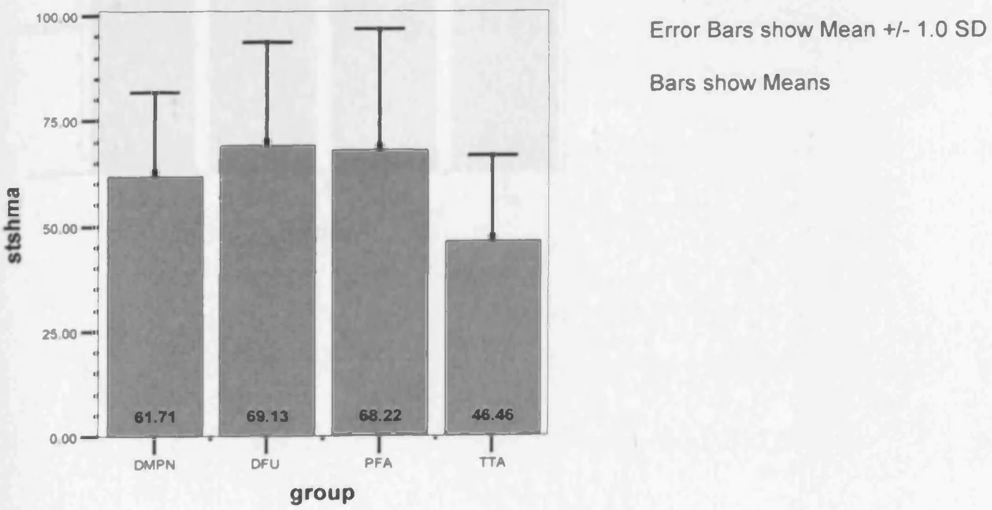


Figure 4.4: Mean values of the net hip moments (N.m) on the affected side during STS (stshma) for the four groups. The error bars present the mean +/- 1.0 S.D.



On the contra-lateral side the ankle (p<0.001) and the hip (p=0.002) showed significant variation between the four groups. Significant linear contrasts indicate a rise in ankle (p<0.001) and the hip (p=0.002) net joint moments across the 4 groups. The TTA group presented the highest net joint moments of the ankle and the hip on the contra-lateral limb as demonstrated in Figure 4.5 & Figure 4.6 respectively.

The knee moments were not different between the four groups (p=0.597) on the contra-lateral limb.

Figure 4.5: Mean values of net ankle moments (N.m) on the contra-lateral side during STS (stsakmn) for the four groups. The error bars present the mean +/- 1.0 S.D.

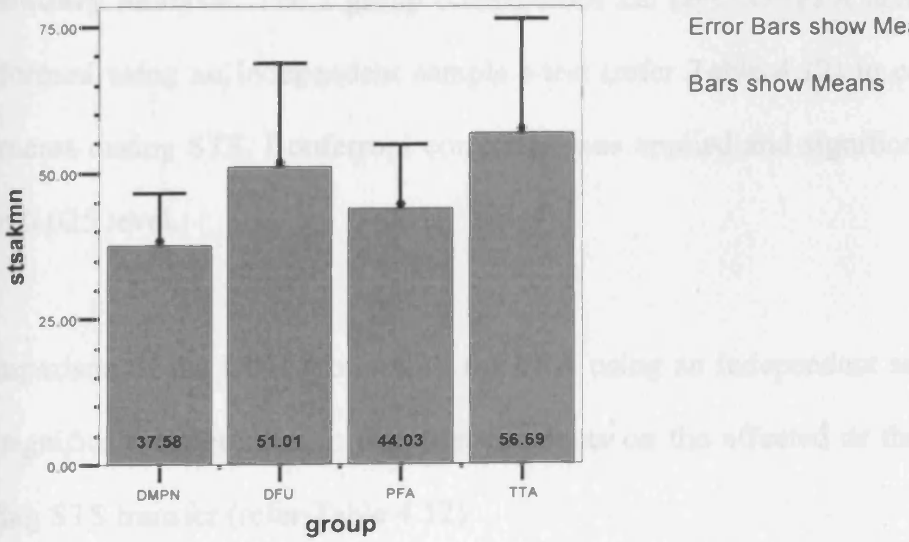
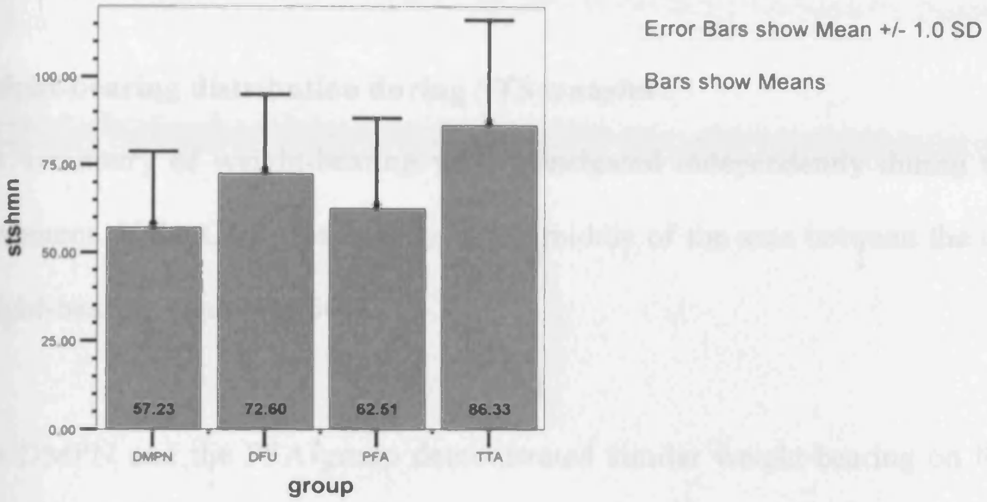


Figure 4.6: Mean values of net hip moments (N.m) on the contra-lateral side during STS (stshmn) for the four groups. The error bars present the mean +/- 1.0 S.D



Secondary analysis: The 2 group comparisons i.e. DFU vs. PFA and PFA vs. TTA were performed using an Independent sample t-test (refer Table 4.12) to compare the net joint moments during STS. Bonferroni correction was applied and significance was determined at p=0.025 level.

Comparison of the DFU group with the PFA using an independent sample t-test revealed no significant differences in the joint moments on the affected or the contra-lateral limb during STS transfer (refer Table 4.12).

Comparison of the PFA and TTA groups using an independent sample t-test revealed significantly lower moments on the affected knee and hip for the TTA group. On the contra-lateral limb the TTA group demonstrated significantly larger ankle and hip joint moments (refer Table 4.12).

Weight-bearing distribution during STS transfer:

The symmetry of weight-bearing was investigated independently during the sit-to-stand movement. If the COP was exactly in the middle of the area between the two ankles, the weight-bearing value was 50%.

The DMPN and the PFA group demonstrated similar weight-bearing on the affected (in case of the DMPN group, the right side was considered as the affected side by default) and the contra-lateral limb during the sit-to-stand movement (Table 4.13). Whereas the majority of the patients (86.4%) from the TTA group demonstrated increased (> 50%) weight-bearing on the contra-lateral limb during the movement. The DFU group was the next group to present with asymmetry, wherein 56.5% of the patients took increased weight on the contra-lateral limb. Data from 1 patient was missing in the DFU group due to technical reasons.

Table 4.13: Symmetry in weight-bearing during sit-to-stand movement

Side of weight-bearing during STS	DMPN n (%)	DFU n (%)	PFA n (%)	TTA n (%)
Affected	12 (52.2)	9 (39.1)	9 (56.3)	3 (13.6)
Contra-lateral	11 (47.8)	13 (56.5)	7 (43.8)	19 (86.4)

n=number of patients %=percentage of patients

4.2B: Quiet standing:

Primary analysis: The group means of the data from the total excursion of the Centre of Pressure (COP) in meter (m) are presented along with the standard deviations. The data from all the four groups were compared using one-way ANOVA revealing a significant difference across the 4 groups (refer to Table 4.14). The F-value is presented with the corresponding degrees of freedom (df) and the total number of patients (n). Significant linear polynomial contrast (p=0.002) indicated a rise in the COP excursion from DMPN to DFU to PFA group (refer to Figure 4.7).

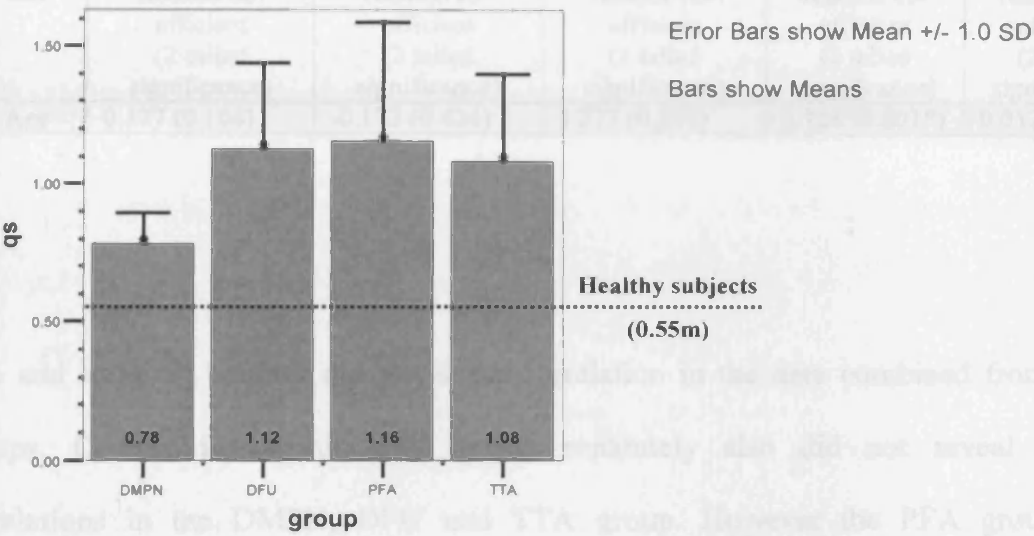
Table 4.14: Comparison of excursion of COP between the 4 groups

Primary analyses							Secondary analyses	
Groups	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	ANOVA $F_{df,n}$	Linear Polynomial contrast	DFU vs PFA t_{df} p value	PFA vs TTA t_{df} p value
COP (m)	0.78 (0.11)	1.12 (0.32)	1.16 (0.43)	1.08 (0.32)	$F_{3,83}$=7.011 p<0.001*	0.079-0.336 p=0.002*	-0.261 26.077 p=0.796	0.616 26.619 p=0.543

Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.

Secondary analysis: The COP excursion was compared between the DFU and PFA groups using an independent sample t-test. The two groups did not show significant difference (p=0.796) (refer Table 4.14). Comparison of COP excursion between the PFA and TTA group did not reveal significant difference either (p=0.543).

Figure 4.7: Comparison of excursion of COP (m) among the 4 groups. The horizontal dotted line presents the standing balance of healthy subjects. On the Y-axis 'qs' refers to the balance during 'Quiet standing'.



Descriptive comparison of the results from the present study with the healthy subjects revealed that there was deterioration in the standing balance from the healthy subjects to the diabetic neuropathic patients (refer Figure 4.7). The data from 10 healthy male subjects (60-64 yrs age) were extracted from the study reported by Ekdahl et al. 1989. The horizontal dotted line refers to the excursion of COP in healthy subjects (0.55m).

The data were investigated for: 1) correlation between age and standing balance using Pearson's co-relation co-efficient (refer to Table 4.15. The values for 2 tailed significance are presented) and 2) neuropathy score and standing balance using one-way ANOVA (Table 4.16).

Table 4.15: Association between quiet standing and age

Quiet standing vs age					
Groups	All 4 grps (n=84)	DMPN (n=23)	DFU (n=23)	PFA (n=16)	TTA (n=22)
Statistic test	Pearson's co-relation co-efficient (2 tailed significance)	Pearson's co-relation co-efficient (2 tailed significance)	Pearson's co-relation co-efficient (2 tailed significance)	Pearson's co-relation co-efficient (2 tailed significance)	Pearson's co-relation co-efficient (2 tailed significance)
Age	0.177 (0.106)	-0.172 (0.434)	0.277 (0.201)	0.726 (0.001*)	0.012 (0.957)

Age and standing balance did not show correlation in the data combined from all the 4 groups. Correlations within each group separately also did not reveal significant correlations in the DMPN, DFU and TTA group. However the PFA group showed significant correlation between the two variables (refer Table 4.15).

Table 4.16: Comparison between quiet standing and neuropathy score

Quiet standing vs neuropathy score					
Groups	Total sample (n=84)	DMPN (n=23)	DFU (n=23)	PFA (n=16)	TTA (n=22)
Statistic test	ANOVA $F_{df,n}$	ANOVA $F_{df,n}$	ANOVA $F_{df,n}$	ANOVA $F_{df,n}$	ANOVA $F_{df,n}$
Neuropathy score	$2.753_{3,83}$ p=0.048*	$3.798_{2,22}$ p=0.040*	$0.608_{2,22}$ p=0.554	$0.475_{3,15}$ p=0.0705	$1.246_{3,21}$ p=0.322

The total sample and the individual groups were divided into 4 subgroups based on the neuropathy score (0,1,2,3) (refer Table 4.16). The difference in the COP excursion was tested using an ANOVA.

There was a significant difference in the quiet standing score (COP excursion) when the total sample and the DMPN group was divided on the basis of the neuropathy score

(0,1,2,3). In the total sample the patients (n=49/84) with complete sensory loss (neuropathy score=0) were most unstable (COP=1.095 m). Similarly in the DMPN group the patients (n=5/23) with complete sensory loss (neuropathy score=0) were most unstable (COP=0.88 m). However the patients with diminished sensory loss (neuropathy score 1, 2 and 3) did not demonstrate a specific trend in their average quiet standing score in the total sample (neuropathy score: quiet standing = 1: 0.936, 2: 0.846 & 3:1.081) and the DMPN group separately (neuropathy score: quiet standing = 1: 0.718; 2: 0.764). There was no significant difference between quiet standing and neuropathy score in the DFU, PFA and TTA groups (refer Table 4.16).

4.2C: Gait:

Spatial (Gait velocity) and temporal parameters (Cadence and stride length) were used along with the kinetic parameters (Net joint moments and the symmetry of weight-bearing force) to analyse gait.

Primary analysis: The group means and standard deviations of the data from cadence, gait velocity and stride length are presented in the Table 4.17. Comparison of all the 4 groups using unrelated ANOVA revealed significant differences.

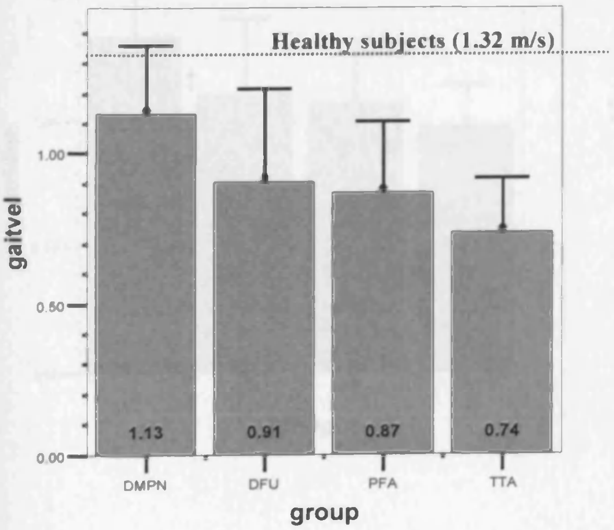
Table 4.17: Comparison of gait velocity, cadence and stride length

Primary analyses							Secondary analyses	
Gait Parameters	**Grp DMPN Mean (SD)**	**Grp DFU Mean (SD)**	**Grp PFA Mean (SD)**	**Grp TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	**DFU vs PFA t_{df} p value**	**PFA vs TTA t_{df} p value**
Gait velocity (m/s)	1.13 (0.22)	0.91 (0.31)	0.87 (0.23)	0.74 (0.18)	$F_{3,81}=10.591$ $p<0.001$*	-0.376 – -0.172 $p<0.001$*	$0.399_{35.000}$ $p=0.692$	$1.933_{26.906}$ $p=0.064$
Cadence (steps/min)	102 (11)	95 (17)	97 (12)	89 (12)	$F_{3,81}=3.736$ $p=0.014$*	-13.665 – -2.615 $p=0.004$*	$-0.433_{34.942}$ $p=0.668$	$2.169_{31.662}$ $p=0.038$
Stride length (m)	1.33 (0.18)	1.11 (0.30)	1.07 (0.24)	0.98 (0.16)	$F_{3,81}=9.789$ $p<0.001$*	-0.338 – -0.147 $p<0.001$*	$0.387_{34.838}$ $p=0.701$	$1.300_{24.419}$ $p=0.206$

Standard Bonferroni correction was applied to adjust the significance level to $p\leq 0.025$.

Gait velocity, cadence and stride length were significantly different between the four groups (refer Table 4.17) demonstrating a gradual decline across the four groups (refer to Figure 4.8, 4.9 & 4.10 respectively). The decline in gait velocity and stride length was smooth from the DMPN to TTA group. Whereas the decrease in the cadence showed a deviation from the linear decline between groups (DFU to PFA).

Figure 4.8: Comparison of gait velocity (m/sec) between the 4 groups.



The horizontal dotted line presents the gait velocity of healthy subjects.

Figure 4.9: Comparison of cadence (steps/min) between the 4 groups

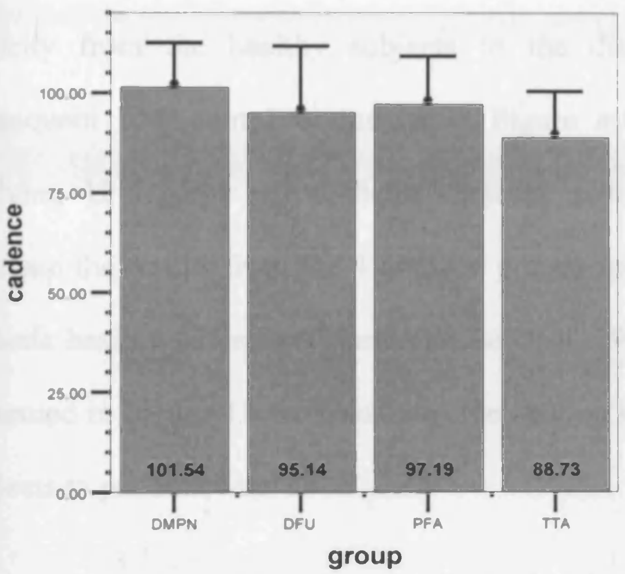
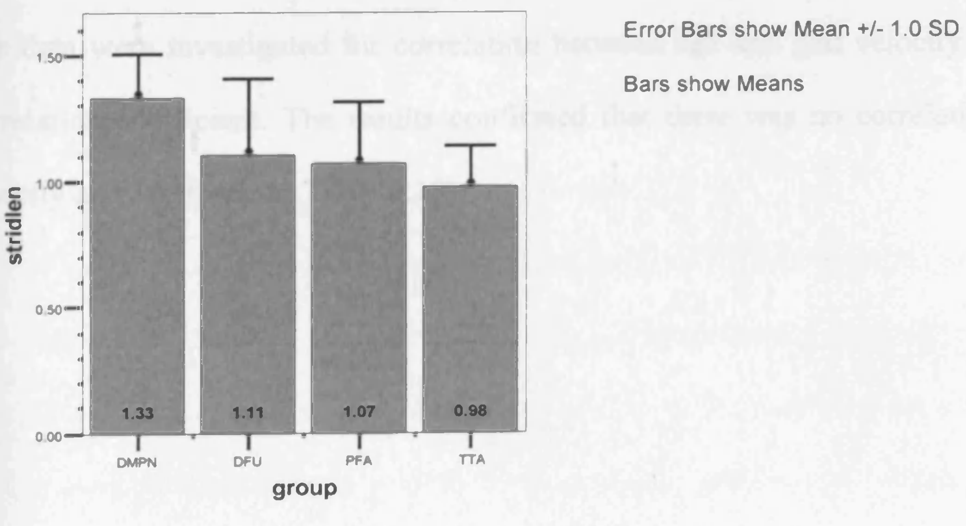


Figure 4.10: Comparison of stride length (m) between the 4 groups



Descriptive comparison of the results of gait velocity from the diabetic neuropathic patients with the healthy subjects (1.32m/sec) demonstrates that there is a decline in the gait velocity from the healthy subjects to the diabetic neuropathic patient groups with consequent foot complications (refer Figure 4.8). The results from a previous report studying 12 healthy non-diabetic subjects with mean age=60.6 yrs were extracted to compare the results from the 4 diabetic groups included in the present study with the non-diabetic healthy subjects (Courtemanche et al. 1996). Graphical comparison of the groups presented in Figure 4.8 demonstrates the decline in gait velocity from healthy non-diabetic subjects to patients with TTA.

Secondary analysis: Gait velocity, cadence and stride length were compared between the DFU vs. PFA and PFA vs. TTA groups using an Independent sample t-test (refer Table 4.17). Comparison of gait velocity, cadence and stride length between the DFU vs. PFA groups and PFA vs. TTA groups did not demonstrate significant differences (refer Table 4.17).

The data were investigated for correlation between age and gait velocity using Pearson's correlation coefficient. The results confirmed that there was no correlation between gait velocity and age (refer to Table 4.18).

Table 4.18: Correlation between gait velocity and age in the four groups

Gait velocity vs age					
Groups	**All 4 groups (n=84)**	**DMPN (n=23)**	**DFU (n=23)**	**PFA (n=16)**	**TTA (n=22)**
Statistic test	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**
Age	-0.094 (0.406)	0.201 (0.359)	-0.427 (0.060)	-0.367 (0.178)	-0.044 (0.847)

Net joint moments:

The peak ankle plantar flexor moments during push-off, the net joint moments at the knee during the loading phase and the peak hip extensor moments during push-off on both sides were used to describe the kinetic characteristics of the gait cycle. The group means and standard deviations of the joint moments on the affected and contra-lateral side are presented in Table 4.19.

Primary analysis: One-way ANCOVA was used to compare the four groups with gait velocity as the co-variate. The gait velocity was measured during the recording of the gait as the subjects walked over the force platform. Linear polynomial contrast was used to test for trends across the four groups (refer Table 4.19).

The joint moments of the ankle ($p<0.001$) and the knee ($p=0.003$) on the affected limb were significantly different between the four groups although the hip moments did not vary. The linear polynomial contrast was significant in case of the ankle moments on the affected limb showing a decline in the joint moments from the DMPN to TTA group. However, the knee moments on the affected limb did not demonstrate a significant trend across the groups.

On the contra-lateral limb the ankle, knee and the hip joint moments did not vary between the four groups (refer Table 4.19).

Secondary analysis: Lower limb joint moments were compared between the DFU vs. PFA and PFA vs. TTA groups using univariate analysis of co-variance using gait velocity as a co-variate (refer Table 4.19). The PFA group demonstrated significantly less peak ankle plantar flexor moments on the affected limb compared to the DFU group (p=0.004).

Compared to the PFA group the TTA group demonstrated significantly higher ankle moments on the prosthetic limb (p=0.004) and significantly lower knee moments on the amputated limb (p=0.005).

Table 4.19: Comparison of joint moments during walking between the 4 groups

Primary analyses							Secondary analyses	
Gait Joint moments (N.m)	**Grp DMPN Mean (SD)**	**Grp DFU Mean (SD)**	**Grp PFA Mean (SD)**	**Grp TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	**DFU vs PFA F_{df} p value**	**PFA vs TTA F_{df} p value**
Ankle (affected)	128.0 (25.2)	111.4 (30.0)	83.0 (21.7)	105.3 (29.4)	$F_{3,80}$=5.093 p=0.003*	-27.456 – -0.107 p=0.048	9.845 $_1$ p=0.004*	9.638 $_1$ p=0.004*
Ankle (contra-lateral)	124.8 (22.2)	131.2 (29.3)	118.5 (26.4)	114.3 (19.9)	$F_{3,80}$=1.181 p=0.323	N.A.	N.A.	N.A.
Knee (affected)	40.7 (12.5)	52.4 (21.4)	55.5 (33.3)	33.3 (13.5)	$F_{3,80}$=4.848 p=0.004*	-12.924 – 8.378 p=0.672	0.038 $_1$ p=0.848	8.812 $_1$ p=0.005*
Knee (contra-lateral)	50.8 (18.8)	43.9 (21.2)	47.2 (28.9)	50.3 (19.7)	$F_{3,80}$=0.924 p=0.433	N.A.	N.A.	N.A.
Hip (affected)	66.9 (19.5)	60.9 (16.9)	53.9 (17.9)	52.5 (15.7)	$F_{3,80}$=0.574 p=0.634	N.A.	N.A.	N.A.
Hip (contra-lateral)	67.9 (23.9)	68.5 (24.1)	59.7 (18.9)	64.4 (32.9)	$F_{3,80}$=0.869 p=0.461	N.A.	N.A.	N.A.
Gait velocity (m/s)	1.13 (0.21)	0.99 (0.19)	0.86 (0.19)	0.80 (0.17)	$F_{3,82}$=12.556 p<0.001*	-0.330 – -0.167 p<0.001*		

N.A.: not applicable **Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.**

Weight-bearing during level walking:

Symmetry of weight-bearing was evaluated during gait using the data from the magnitude of ground reaction force (GRF). Peak pressure (MPP), Pressure-time integral (PTI) and daily plantar cumulative stress (DPCS) were used to describe plantar pressure distribution during level walking. Considering the influence of gait speed on peak pressures (Burnfield et al. 2004), gait velocity was used as a co-variate in the comparison of MPP, PTI & DPCS across the 4 groups using Uni-variate ANCOVA.

Symmetry of weight-bearing:

The force of weight-bearing on both the lower limbs during walking is presented in Newton. Additionally the force of weight-bearing is presented in terms of percentage of the total body weight expressed in Newton. The descriptive statistics for the results are presented in Table 4.20 along with the results for ANOVA and linear polynomial contrast.

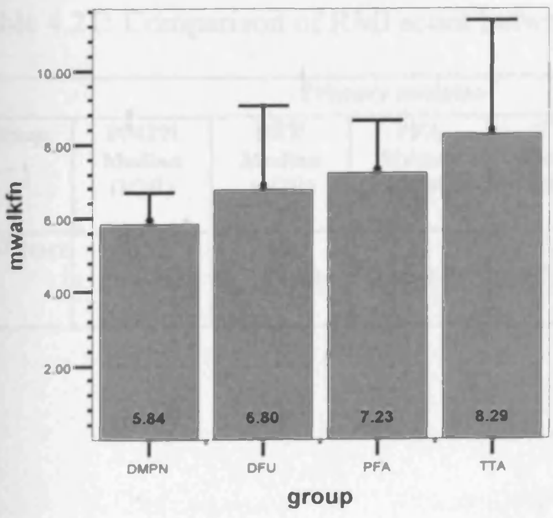
Table 4.20: Comparison of the magnitude of GRF (N) on the affected and unaffected limb during walking between the 4 groups

Primary analyses							Secondary analyses	
Side of weight-bearing during gait	**DMPN Mean (S.D.)**	**DFU Mean (S.D.)**	**PFA Mean (S.D.)**	**TTA Mean (S.D.)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	DFU vs PFA t_{df} p value	PFA vs TTA t_{df} p value
Affected (N)	556.3 (123.5)	615.8 (157.4)	644.6 (175.0)	633.8 (109.4)	$F_{3,82}$=1.663 p=0.182	N.A.	N.A.	N.A.
Weight-bearing force (N) / Body Weight (N)	0.6 (0.1)	0.7 (0.2)	0.7 (0.1)	0.7 (0.1)	$F_{3,80}$=1.550 p=0.208	N.A.	N.A.	N.A.
Contra-lateral (N)	546.3 (113.9)	653.0 (185.9)	678.5 (175.8)	784.1 (270.9)	$F_{3,80}$=5.596 p=0.002*	82.150 – 248.262 p<0.001*	$-0.519_{30.503}$ p=0.674	$0.497_{24.513}$ p=0.623
Weight-bearing force (N) / Body weight (N)	0.6 (0.1)	0.7 (0.2)	0.7 (0.1)	0.8 (0.3)	$F_{3,80}$=5.186 p=0.003*	0.086 – 0.268 p<0.001*	$-0.707_{34.051}$ p=0.484	$-1.425_{31.536}$ p=0.164

N.A.: not applicable

Primary analysis: On the affected limb the 4 groups [in case of the DMPN group the right lower limb was considered as the affected limb by default. Although there was a significant difference in the weight-bearing force between the right and the left lower limb (p=0.038), the results of the ANOVA and the linear contrast for the 4 groups remained exactly the same irrespective of the side chosen as the affected or contra-lateral side for the DMPN group] did not vary significantly in the force of weight-bearing (p=0.182, p=0.208). Whereas on the contra-lateral limb there was a significant difference between the 4 groups demonstrating a steady rise in the force of weight-bearing with the progression of foot complications from neuropathy alone to TTA (refer Figure 4.11). The DMPN group walked with 0.6 times the body weight whereas the TTA group walked with 0.8 times the body weight (refer Table 4.20) on the contra-lateral limb during walking.

Figure 4.11: Steady rise in the force of weight-bearing (N) on the contra-lateral limb during walking (i.e. 'mwalkfn' on the y-axis) across the 4 groups



Secondary analysis: Specific group comparison revealed no significant difference in the weight-bearing force on the contra-lateral limb (p=0.674, p=0.484) during walking between the DFU vs PFA groups (refer Table 4.20). Comparison between the PFA vs TTA groups also did not reveal any significant difference in the weight-bearing force on the contra-lateral limb (p=0.154, p=0.164) during walking (refer Table 4.20).

4.3: Self-reported measure of mobility: RMI

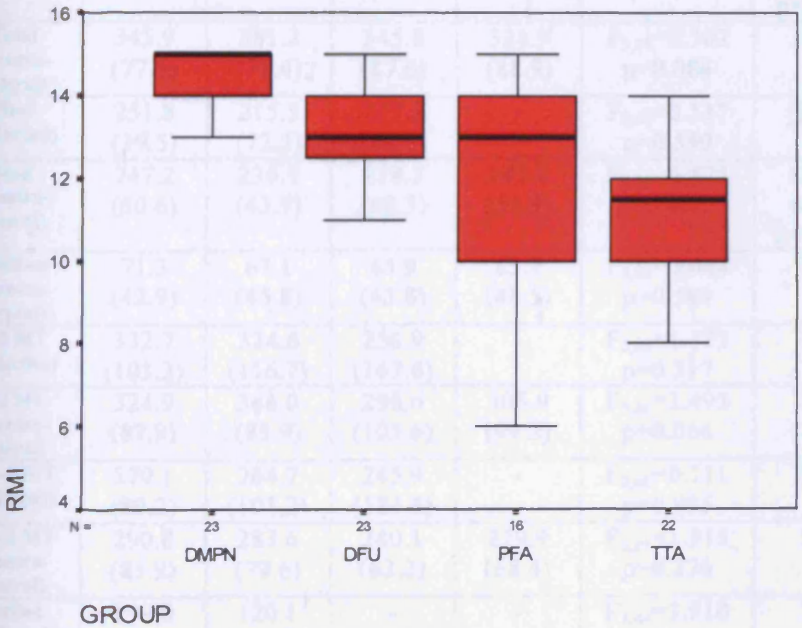
Primary analysis: The 4 groups were compared using the Kruskal Wallis test which showed significant difference (p<0.001) across groups in their RMI score. The median was used as a measure of central tendency and the interquartile range (the range between 25th and 75th percentile) was used as a measure of their variability (refer Table 4.21). The Figure 4.12 demonstrates the decline in the RMI score across the four groups. Higher score indicates better mobility.

Table 4.21: Comparison of RMI score between the 4 groups

Primary analyses						Secondary analyses	
Group	**DMPN Median (IQR)**	**DFU Median (IQR)**	**PFA Median (IQR)**	**TTA Median (IQR)**	**Kruskal Wallis Chi-square$_{df}$ p value**	**DFU vs PFA Z p value**	**PFA vs TTA Z p value**
RMI score	15 (14-15)	13 (12-14)	13 (10-14)	11.5 (9.75-12)	30.846_3 p<0.001*	-1.658 p=0.097	-1.553 p=0.120

Secondary analysis: The RMI score was compared between DFU vs. PFA & PFA vs. TTA groups using the Mann-Whitney test. There was no significant difference between the three groups (refer Table 4.21).

Figure 4.12: Comparison of the RMI score for the four groups. The range of the RMI scores are presented in the box plots



4.4: Plantar pressure distribution:

Primary analysis: The group means along with the standard deviations of MPP (kPa) over the total foot surface area and various regions of the foot on both the sides are presented in Table 4.22. The means of the 3 groups (DMPN, DFU & PFA) were compared using One-way ANCOVA on the affected limb and the means of all the 4 groups were compared.

Linear polynomial contrast was used to investigate the trend across the four groups in case of significant ANOVA.

Table 4.22: Comparison of MPP (kPa) between the 4 groups

Primary analyses							Secondary analyses	
MPP (kPa) Foot regions	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear contrast**	DFU vs PFA F_{df} p value	PFA vs TTA F_{df} p value
Total (affected)	356.4 (88.9)	359.2 (70.8)	400.3 (108.0)	-	$F_{2,60}$=3.313 p=0.044*	11.652-95.245 p=0.013*	3.031_1 p=0.091	-
Total (contra-lateral)	345.9 (77.8)	381.2 (71.4)	345.8 (87.6)	336.9 (88.9)	$F_{3,81}$=2.302 p=0.084	N.A.	N.A.	N.A.
Heel (affected)	251.8 (39.5)	215.5 (72.2)	217.2 (64.9)	-	$F_{2,60}$=0.517 p=0.599	N.A.	N.A.	-
Heel (contra-lateral)	247.2 (50.6)	236.9 (43.9)	278.2 (68.3)	245.8 (52.9)	$F_{3,81}$=4.825 p=0.004*	12.621-60.266 p=0.003*	6.065_1 p=0.019*	0.961_1 p=0.334
Midfoot (contra-lateral)	71.3 (42.9)	67.1 (45.8)	65.9 (43.8)	83.7 (48.5)	$F_{3,81}$=0.644 p=0.589	N.A.	N.A.	N.A.
1-2 MT (affected)	332.7 (103.2)	324.6 (116.7)	256.9 (167.6)	-	$F_{2,60}$=1.173 p=0.317	N.A.	N.A.	-
1-2 MT (contra-lateral)	324.9 (87.9)	366.0 (88.9)	298.6 (105.6)	305.9 (99.2)	$F_{3,81}$=2.493 p=0.066	N.A.	N.A.	N.A.
3-4-5 MT (affected)	279.1 (89.2)	264.7 (101.2)	245.9 (184.6)	-	$F_{2,60}$=0.111 p=0.895	N.A.	N.A.	-
3-4-5 MT (contra-lateral)	290.8 (81.9)	283.6 (79.6)	240.1 (62.2)	229.9 (68.4)	$F_{3,81}$=1.315 p=0.276	N.A.	N.A.	N.A.
Hallux (affected)	199.0 (96.9)	120.1 (118.5)	-	-	$F_{1,44}$=3.910 p=0.055	N.A.	-	-
Hallux (contra-lateral)	182.9 (77.7)	187.2 (108.3)	147.5 (105.5)	157.7 (115.5)	$F_{3,81}$=0.431 p=0.731	N.A.	N.A.	N.A.
Toes (affected)	123.4 (72.3)	59.0 (52.9)	14.6 (31.4)	-	$F_{2,60}$=15.560 p<0.001*	-107.569--50.225 p<0.001*	9.159_1 p=0.005*	-
Toes (contra-lateral)	110.6 (71.2)	73.5 (40.4)	70.5 (48.1)	86.9 (54.9)	$F_{3,81}$=1.857 p=0.144	N.A.	N.A.	N.A.

N.A.: not applicable **Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.**

On the affected limb, the peak pressures over the total foot area (p=0.044) and the region of toes (p<0.001) were significantly different between the 3 groups. The significant contrast demonstrated the rise in MPP over the total foot area (p=0.013) from the DMPN to DFU to PFA group. However the region of the toes (p<0.001) demonstrated a significant decline in the MPP from the DMPN to DFU to PFA group (refer Table 4.22). The significant difference in the MPP over the toe region might be due to an artefact as the peak pressures were not recorded in that region since most patients of the PFA group had toe amputations. Despite walking slower the PFA group presented with highest pressures over the total foot area (refer Figure 4.13 & Figure 4.14) demonstrating the impact of PFA on the plantar pressure distribution. Since the data were not normally distributed for the MPP over the affected midfoot, Kruskal-Wallis test was performed for this variable. There was no significant difference in the MPP over the midfoot between the 3 groups (p=0.241).

Figure 4.13: MPP (kPa) between the 3 groups over the total foot area on the affected limb (apptotl)

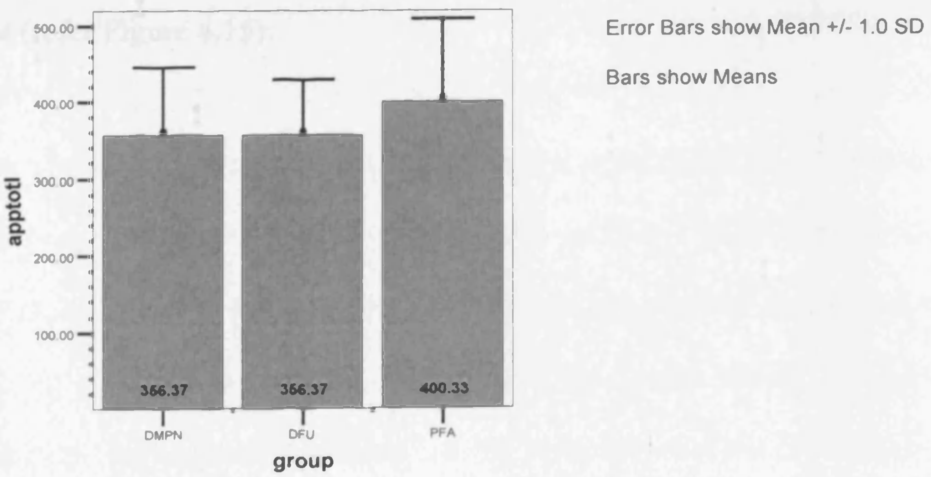
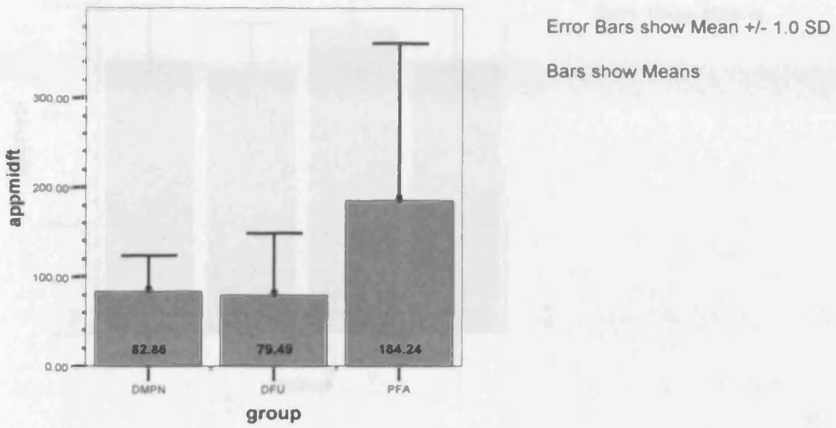
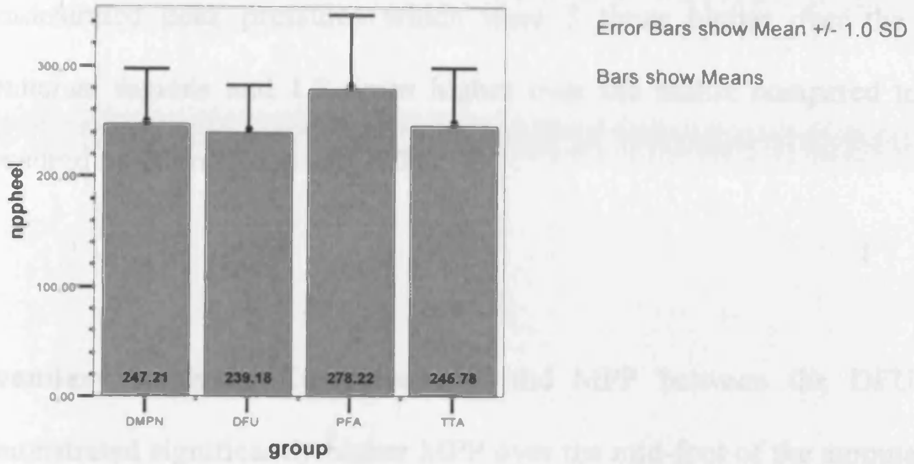


Figure 4.14: MPP (kPa) over the mid-foot of the affected limb between the 3 groups (appmidft)



On the contra lateral limb the four groups showed a significant difference in MPP over the heel region (p=0.004). The significant linear contrast demonstrated a significant trend across the groups (p=0.003). Graphical comparison of the group means revealed that the PFA group demonstrated the maximum peak pressures over the heel of the contra-lateral foot (refer Figure 4.15).

Figure 4.15: MPP (kPa) over the heel of the contra-lateral limb between the 4 groups (nppheel)



Descriptive comparison of the average MPP of the DMPN group of the present study with the healthy subjects studied by Burnfield et al. 2004 confirm that the peak pressures increase with DMPN (Katoulis, Boulton & Raptis 1996). Burnfield et al (2004) documented MPP of 110 kPa over the medial MT, 130 kPa over the central MT, 90 kPa over the lat MT and 120 kPa over the hallux from 20 healthy adults walking at a speed of 1.33m/s (average height=170.9 cm; body mass=78.5 kg) measured with Pedar in-shoe pressure measurement system (Burnfield, Few, Mohamed & Perry 2004). The DMPN group (n=23) of the present study walked at a speed of 1.13 m/s resulting in MPP of 332.68 kPa over the 1-2 MTP, 279.09 kPa over the 3-4-5 MTP, 199.03 kPa over the hallux (average height=174.7 cm, body mass=93.2 kg). As the same equipment was used to analyse pressures it was reasonable to compare the results between the two studies. However, the interpretation based on the comparison of the MPP between the two groups needs to be made with the understanding that the DMPN group was 1.2 times heavier and walked at a speed of 0.20 m/s slower compared to the healthy adults. The average MPP was 66.7% higher over the med MT, 67.8% higher over the lat MT and 39.7% higher over the hallux in the DMPN group. Effectively the DMPN group of the present study demonstrated peak pressures which were 3 times higher over the medial and lateral metatarsal regions and 1.7 times higher over the hallux compared to the healthy adults measured by Burnfield et al. (2004).

Secondary analysis: Comparison of the MPP between the DFU and PFA groups demonstrated significantly higher MPP over the mid-foot of the amputated foot of the PFA group and significantly lower MPP over the toe region compared to the DFU group. On the contra-lateral foot, the heel of the PFA group showed higher MPP compared to the DFU group (refer Table 4.22).

Comparison between the PFA and TTA groups did not demonstrate any significant differences in the MPP on the contra-lateral foot (refer Table 4.22).

Pressure-Time Integral (PTI): PTI was compared on the affected and the contra-lateral foot over the six areas of interest between the four groups.

Primary analysis: The group means along with the standard deviations of PTI (kPa.sec) over the total foot surface area and various regions of the foot on both the sides are presented in Table 4.23. The means of the 4 groups were compared using One- way ANCOVA. The F-values are presented with the corresponding degrees of freedom (df) and the total number of patients (n). Linear polynomial contrast was used to examine the trend in PTI across the 4 groups.

The DFU group demonstrated a low PTI value over the hallux of the affected foot compared to the DMPN group ($p=0.012$). The PTI was significantly different over the toes ($p<0.001$) across the 3 groups demonstrating a significant decline in PTI over the toes from DMPN to PFA groups ($p<0.001$) (refer Table 4.23). This significant finding could be an artefact due to the lack of data from the toe region in the PFA group, which included patients with toe amputations.

On the contra-lateral foot, the heel region showed a significant variation ($p=0.041$) and a steady rise ($p=0.008$) in PTI across the 4 groups.

Secondary analysis: Comparison of the PTI between the DFU and PFA groups demonstrated significantly low PTI over the toe region of the affected foot (refer Table 4.23) which may be an artefact due to the toes missing in the PFA group. Comparison of PTI between the PFA and TTA groups on the contra-lateral foot did not demonstrate any significant differences.

Table 4.23: Comparison of PTI (kPa.sec) between the 4 groups

	Primary analyses						Secondary analyses	
PTI (kPa.sec) Foot regions	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	**DFU vs PFA F_{df} p value**	**PFA vs TTA F_{df} p value**
Total (affected)	134.7 (36.9)	156.7 (39.3)	151.6 (47.3)	-	$F_{2,60}$=0.270 p=0.764	N.A.	N.A.	-
Total (contra-lateral)	134.7 (36.9)	160.2 (37.3)	150.9 (42.9)	179.9 (39.6)	$F_{3,81}$=1.415 p=0.245	N.A.	N.A.	N.A.
Heel (affected)	64.4 (13.9)	75.6 (38.8)	71.0 (26.0)	-	$F_{2,60}$=0.325 p=0.724	N.A.	N.A.	-
Heel (contra-lateral)	65.8 (12.2)	77.1 (26.8)	88.9 (30.9)	103.3 (26.0)	$F_{3,81}$=2.895 p=0.041*	3.849-25.248 p=0.008*	1.636_1 p=0.210	1.008_1 p=0.322
Midfoot (affected)	24.5 (17.2)	29.8 (28.8)	57.2 (61.8)	-	$F_{2,60}$=2.584 p=0.084	N.A.	N.A.	-
Midfoot (contra-lateral)	21.7 (17.9)	22.0 (15.2)	21.5 (16.2)	32.8 (19.9)	$F_{3,81}$=1.264 p=0.293	N.A.	N.A.	N.A.
1-2 MT (affected)	84.1 (37.1)	103.3 (52.7)	76.6 (51.2)	-	$F_{2,60}$=1.692 p=0.193	N.A.	N.A.	-
1-2 MT (contra-lateral)	80.9 (29.6)	123.9 (71.6)	94.2 (41.3)	110.9 (43.2)	$F_{3,81}$=1.898 p=0.137	N.A.	N.A.	N.A.
3-4-5 MT (affected)	73.9 (27.7)	94.2 (54.6)	83.2 (61.3)	-	$F_{2,60}$=0.405 p=0.669	N.A.	N.A.	-
3-4-5 MT (contra-lateral)	77.8 (30.9)	99.4 (40.3)	78.5 (22.3)	91.0 (37.7)	$F_{3,81}$=1.917 p=0.134	N.A.	N.A.	N.A.
Hallux (affected)	33.9 (18.9)	18.7 (19.0)	-	-	$F_{1,44}$=6.832 p=0.012*	-20.647- -2.648 p=0.012*	-	-
Hallux (contra-lateral)	30.6 (14.9)	30.8 (14.7)	24.6 (19.2)	45.3 (41.4)	$F_{3,81}$=1.876 p=0.141	N.A.	N.A.	N.A.
Toes (affected)	26.4 (19.3)	12.5 (8.9)	2.7 (6.2)	-	$F_{2,60}$=16.655 p<0.001*	-25.457- -12.183 p<0.001*	13.399_1 p<0.001*	-
Toes (contra-lateral)	21.2 (15.5)	18.7 (13.3)	17.0 (14.0)	28.1 (24.3)	$F_{3,81}$=1.241 p=0.301	N.A.	N.A.	N.A.

N.A.: not applicable **Standard Bonferroni correction was applied to adjust the significance level to $p \leq 0.025$.**

Daily Plantar Cumulative Stress (DPCS):

The group means along with the standard deviations of DPCS (MPa/day) over the total foot surface area and various regions of the foot on both sides are presented in Table 4.24. DPCS is a product of average daily strides and PTI. The results of the strides/day are presented in the domain of performance of activity however they are presented here as a component of DPCS.

Primary analysis: The means of the 4 groups were compared using One- way ANCOVA. The F-values are presented with the corresponding degrees of freedom (df) and the total number of patients (n). Linear polynomial contrast was used to investigate the trend in the DPCS across the 4 groups (refer Table 4.24).

Despite significant differences in average daily strides between the four groups, the daily plantar cumulative stress over the total surface area of the foot did not vary significantly between the four groups. On the affected foot, the hallux ($p=0.007$) and toe region ($p<0.001$) demonstrated significant difference in DPCS (refer Table 4.24). The DPCS showed a significant reduction from DMPN to PFA group over the toe region ($p<0.001$) whereas the DFU group demonstrated significantly lower DPCS over the hallux compared to the DMPN group ($p=0.007$). In case of the toe region, the three groups were not uniform because some of the patients of the PFA group had amputation of the toes. Therefore, the significant difference between the 4 groups over the toe region may be considered as an artefact.

On the contra-lateral foot the DPCS was significantly different on the lateral metatarsal region (3-4-5 MTP) between the groups ($p=0.028$) demonstrating a significant decline ($p=0.005$).

Table 4.24: Comparison of DPCS (MPa/day) across the 4 groups

Primary analyses							Secondary analyses	
DPCS (MPa/day) Foot regions	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	DFU vs PFA F_{df} p value	PFA vs TTA F_{df} p value
Total (affected)	5794.9 (2705.4)	4807.7 (3196.8)	4592.2 (2092.7)	-	$F_{2,57}$=0.587 p=0.560	N.A.	N.A.	-
Total (contra-lateral)	5794.9 (2705.4)	5056.8 (3684.8)	4588.7 (1735.3)	3457.8 (2105.5)	$F_{3,78}$=1.482 p=0.227	N.A.	N.A.	N.A.
Heel (affected)	2781.9 (1204.4)	2177.5 (1722.1)	2246.0 (1248.9)	-	$F_{2,57}$=0.994 p=0.377	N.A.	N.A.	-
Heel (contra-lateral)	2897.4 (1430.6)	2341.9 (1596.1)	2711.2 (1047.6)	2021.1 (1348.5)	$F_{3,78}$=1.048 p=0.377	N.A.	N.A.	N.A.
Midfoot (affected)	1020.9 (8096.8)	8670.2 (8339.2)	1390.5 (1348.5)	-	$F_{2,57}$=1.158 p=0.322	N.A.	N.A.	-
Midfoot (contra-lateral)	8358.3 (6338.3)	6560.9 (5789.8)	5530.9 (4262.3)	7098.2 (6741.1)	$F_{3,78}$=0.594 p=0.621	N.A.	N.A.	N.A.
1-2 MT (affected)	3586.1 (2077.7)	3290.1 (2982.4)	2638.3 (2031.4)	-	$F_{2,57}$=0.472 p=0.626	N.A.	N.A.	-
1-2 MT (contra-lateral)	3540.7 (2064.2)	3809.7 (2944.6)	2913.7 (1379.6)	2090.7 (1492.9)	$F_{3,78}$=2.260 p=0.089	N.A.	N.A.	N.A.
3-4-5 MT (affected)	3163.9 (1677.2)	2877.9 (2308.7)	2558.0 (2078.6)	-	$F_{2,57}$=0.303 p=0.740	N.A.	N.A.	-
3-4-5 MT (contra-lateral)	3293.4 (1708.5)	3233.1 (2746.9)	2389.2 (1182.5)	1647.2 (1051.7)	$F_{3,78}$=3.199 p=0.028*	-223.72 – -414.18 p=0.005*	1.212_1 p=0.279	3.339_1 p=0.077
Hallux (affected)	1443.4 (1074.5)	586.2 (615.2)	-	-	$F_{1,42}$=8.007 p=0.007*	-105.89 – -176.11 p=0.007*	-	-
Hallux (contra-lateral)	1282.9 (8797.1)	9562.9 (8388.7)	7436.4 (7479.3)	8644.3 (8294.9)	$F_{3,78}$=0.851 p=0.470	N.A.	N.A.	N.A.
Toes (affected)	1122.3 (1104.5)	426.9 (387.1)	92.2 (216.2)	-	$F_{2,57}$=9.264 P<0.001*	-116.50 – -404.48 p<0.001*	9.086_1 p=0.005 *	-
Toes (contra-lateral)	877.3 (725.9)	772.6 (100.5)	451.7 (375.8)	585.6 (630.3)	$F_{3,78}$=1.016 p=0.391	N.A.	N.A.	N.A.

N.A.: not applicable **Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.**

Secondary analysis: There was no significant difference in the DPCS between the three groups except that the PFA group demonstrated significantly low DPCS over the region of the toes of the PFA group compared to the DFU group on the affected foot (refer Table 4.24).

4.5: Activity level:

4.5A: Capacity:

The capacity to perform the activity was measured using the Total Heart Beat Index (THBI).

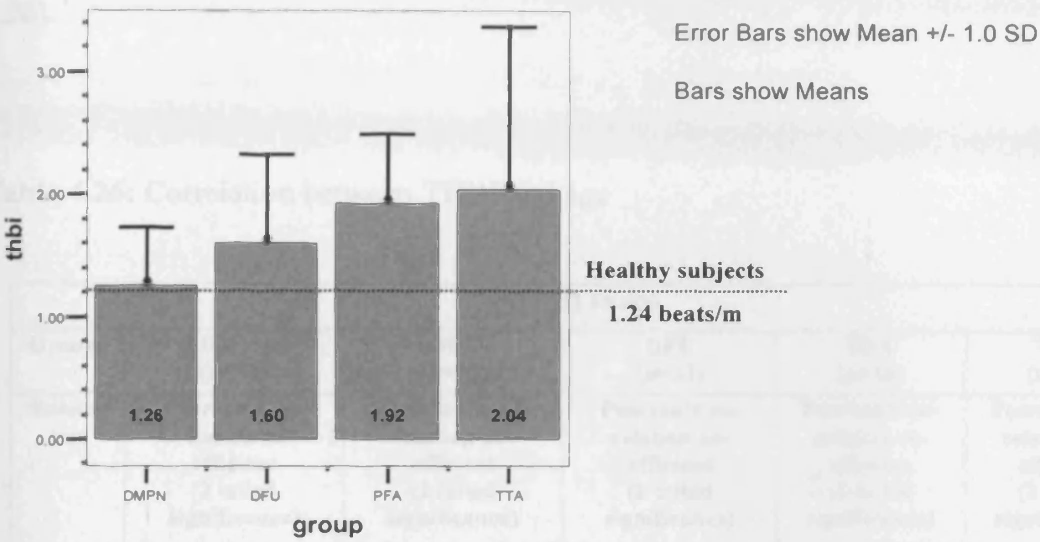
Primary analysis: The mean and SD of the THBI score are presented in Table 4.25. The four groups were significantly different (p=0.018) demonstrating a significant steady rise in the THBI score from DMPN to TTA (p=0.002). The gradual rise in the score across the 4 groups is demonstrated in Figure 4.18 indicating a worsening of the capacity.

Table 4.25: Comparison of THBI score (beats/m) between the four groups

Primary analyses							Secondary analyses	
Groups	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	**DFU vs PFA t_{df} p value**	**PFA vs TTA t_{df} p value**
THBI (beats/m)	1.26 (0.48)	1.60 (0.73)	1.92 (0.57)	2.04 (1.33)	$F_{2,57}$=3.550 p=0.018*	p=0.002*	$-1.471_{33.675}$ p=0.151	$-0.356_{27.213}$ p=0.724

Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.

Figure 4.16: Comparison of THBI score (beats/m) between the 4 groups. The horizontal dotted line presents the THBI score from healthy subjects (1.24 beats/m).



Descriptive comparison of results from the diabetic neuropathic groups with the healthy controls revealed that the mean value of the DMPN group was very close to the mean THBI score of the healthy non-diabetic subjects (refer Figure 4.16). To allow a reference to the THBI score in healthy non-diabetic subjects, the mean THBI score (1.24 beats/m) obtained from 20 subjects (mean age=26.6 ±6.3 yrs) reported by Hood et al. (2002) was used to plot a horizontal dotted line presenting the results from the 4 diabetic groups of the present study (refer Figure 4.16).

Secondary analysis: THBI was compared between the three groups using independent sample t-test. Specific group comparisons i.e. DFU vs PFA and PFA vs TTA did not reveal difference in the THBI score (refer Table 4.25).

Considering the association between age and physical capacity the data were investigated for correlation between age and THBI using Pearson's correlation coefficient. The results confirmed that there was no correlation between the THBI score and age (refer to Table 4.26).

Table 4.26: Correlation between THBI and age

THBI vs age					
Groups	**All 4 grps (n=84)**	**DMPN (n=23)**	**DFU (n=23)**	**PFA (n=16)**	**TTA (n=22)**
Statistic test	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**
Age	0.018 (0.872)	-0.225 (0.302)	0.235 (0.305)	0.098 (0.728)	0.023 (0.923)

4.5B: Performance:

The performance of daily walking activity was recorded in terms of average daily strides.

Primary analysis: The mean values and SD of the average daily strides are presented in Table 4.27. One-way ANOVA revealed overall difference between the groups ($p<0.001$). Significant linear polynomial contrast across the groups ($p<0.001$) demonstrated a decline in average daily strides from DMPN to TTA. However, the PFA group mean was marginally higher than the DFU group (refer Figure 4.17).

Table 4.27: Comparison of average daily strides between the 4 groups

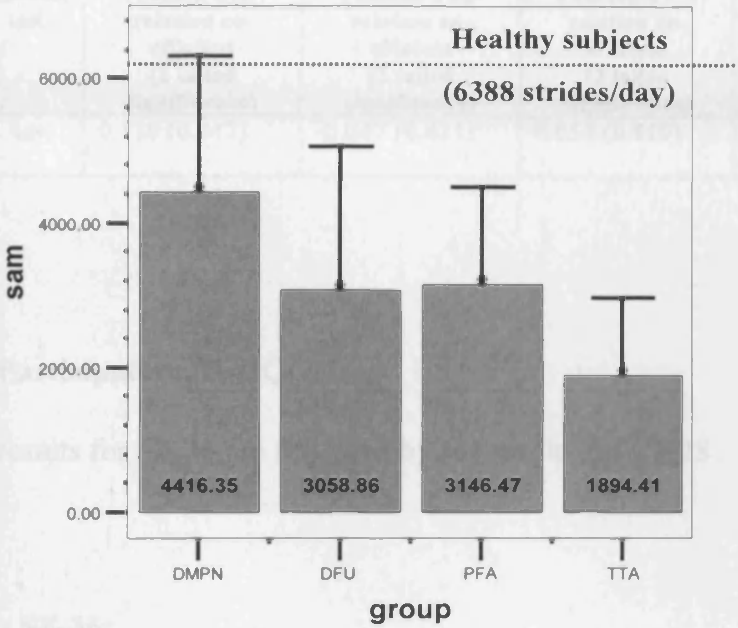
Groups	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	ANOVA $F_{df,n}$	Linear polynomial contrast	DFU vs PFA t_{df} p value	PFA vs TTA t_{df} p value
Average daily strides	4416 (1896)	3058 (1994)	3146 (1360)	1894 (1081)	$F_{3,80}$=8.803 p<0.001*	p<0.001*	-0.157 $_{33.958}$ p=0.876	2.980 $_{25.499}$ p=0.006*

Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.

Descriptive comparison of the results from the diabetic neuropathic groups of the present study with the findings from the normal healthy subjects demonstrated a decline of daily walking performance from healthy non-diabetic subjects (6388 strides/day) to diabetic neuropathic patients (refer Figure 4.17). Busse et al. (2004) studied 27 non-diabetic healthy subjects with mean age of 60.7 yrs. Exactly similar method of measurement of average daily strides between the two studies allowed a fair comparison of the results. The horizontal dotted line presents the daily walking performance of healthy subjects (refer Figure 4.17).

Secondary analysis: Average daily strides were compared between the three groups using Independent sample t-test. There was no significant difference between the DFU and PFA groups. However the TTA group walked significantly less compared to the PFA group (p=0.006) (refer Table 4.27).

Figure 4.17: Comparison of average daily strides between the 4 groups. The horizontal dotted line presents the average daily strides of healthy subjects (6388 strides/day).



Performance of physical activity is known to be affected by the age (Savinainen, Nygard, & Ilmarinen 2004). Therefore, the data were investigated for correlation between age and average daily strides using Pearson's correlation coefficient. The results confirm that there was no correlation between the performance of walking and the age of the diabetic patients with foot complications (refer Table 4.28).

Table 4.28: Correlation between age and average daily strides

Average daily strides vs age					
Groups	**All 4 grps (n=84)**	**DMPN (n=23)**	**DFU (n=23)**	**PFA (n=16)**	**TTA (n=22)**
Statistic test	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**	**Pearson's co-relation co-efficient (2 tailed significance)**
Age	0.130 (0.247)	-0.047 (0.831)	0.053 (0.819)	0.325 (0.238)	-0.018 (0.936)

4.6: Participation: H-RQOL

The results for SF-36 are followed by the results for CWIS.

4.6A: SF-36:

The results for primary and secondary analysis are presented in Table 4.29. Higher scores indicate better function in all the domains.

Primary analysis:

SF-36: Physical Function (PF): The physical function as scored by SF-36 varied significantly between the 4 groups (p=0.002) (refer Table 4.29). The significant linear contrast indicates a decline in the physical function from DMPN to DFU to PFA to TTA groups (refer Figure 4.18).

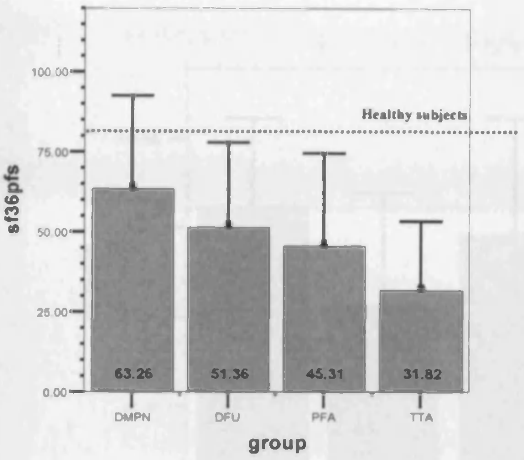
Descriptive comparison of the results from the present study with the healthy subjects demonstrates a decline in Physical function from healthy subjects to diabetic patient groups indicated by a horizontal dotted line plotted in Figure 4.18.

Table 4.29: Results for all the 9 domains of SF-36

Primary analyses							Secondary analyses	
Groups	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**	**DFU vs PFA t_{df} p value**	**PFA vs TTA t_{df} p value**
SF-36 PF (score)	63.26 (29.37)	51.36 (26.51)	45.31 (29.41)	31.82 (21.58)	$F_{3,82}$=5.349 p=0.002*	F=15.513 p<0.001*	0.653 $_{30.388}$ p=0.519	1.556 $_{26.178}$ p=0.132
SF-36 SF (score)	81.31 (24.82)	53.44 (31.94)	73.61 (32.93)	58.08 (28.88)	$F_{3,80}$=4.120 p=0.009*	F=3.032 p=0.086	-1.870 $_{31.912}$ p=0.071	1.511 $_{29.811}$ p=0.141
SF-36 RPS (score)	55.68 (42.21)	28.41 (37.24)	43.33 (46.74)	15.48 (23.02)	$F_{3,79}$=4.564 p=0.005*	F=8.299 p=0.005*	-1.033 $_{25.550}$ p=0.311	2.131 $_{18.874}$ p=0.046
SF-36 RES (score)	66.67 (42.16)	43.48 (45.43)	64.44 (46.23)	53.03 (38.02)	$F_{3,80}$=1.319 p=0.274	N.A.	N.A.	N.A.
SF-36 MH (score)	76.18 (19.73)	71.43 (19.69)	77.75 (18.12)	74.29 (17.09)	$F_{3,79}$=0.404 p=0.751	N.A.	N.A.	N.A.
SF-36 EVS (score)	50.23 (25.66)	44.29 (22.60)	51.56 (25.67)	40.71 (22.82)	$F_{3,79}$=0.869 p=0.461	N.A.	N.A.	N.A.
SF-36 PS (score)	64.65 (30.21)	52.02 (26.42)	55.56 (28.79)	52.02 (24.82)	$F_{3,80}$=1.030 p=0.384	N.A.	N.A.	N.A.
SF-36 GHP (score)	57.00 (23.45)	41.27 (25.23)	52.50 (24.48)	40.68 (24.69)	$F_{3,78}$=2.292 p=0.085	N.A.	N.A.	N.A.
SF-36 CHS (score)	47.83 (16.71)	41.30 (26.77)	56.25 (21.41)	54.55 (28.49)	$F_{3,83}$=1.686 p=0.177	N.A.	N.A.	N.A.

Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.
N.A.: Due to non-significant result from the ANOVA further specific group comparison was not performed.

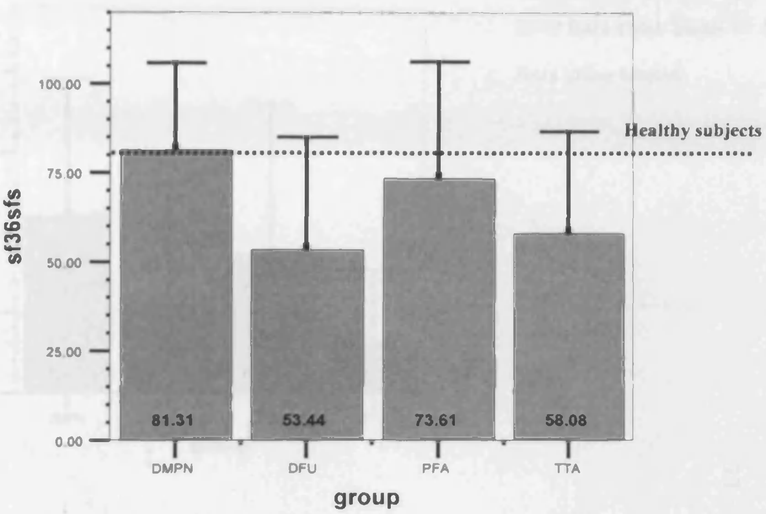
Figure 4.18: Comparison of SF-36 Physical Function (sf36pfs) between the 4 groups



Social function (SF): The four groups demonstrated a significant difference in their social function. The linear polynomial contrast was non-significant leading to acceptance of the null hypothesis that there was no significant decline in social function across the four groups from DMPN to DFU to PFA to TTA (refer Table 4.29). The DFU group demonstrated the lowest score followed by the TTA group and then the PFA group compared to the DMPN (refer Figure 4.19). Graphical comparison of the four group means reveals a 34.3% reduction in the social function of the DFU group compared to the DMPN group. However, the PFA group demonstrated a 27.4% greater social function compared to the DFU group and a 21.1% rise compared to the TTA group.

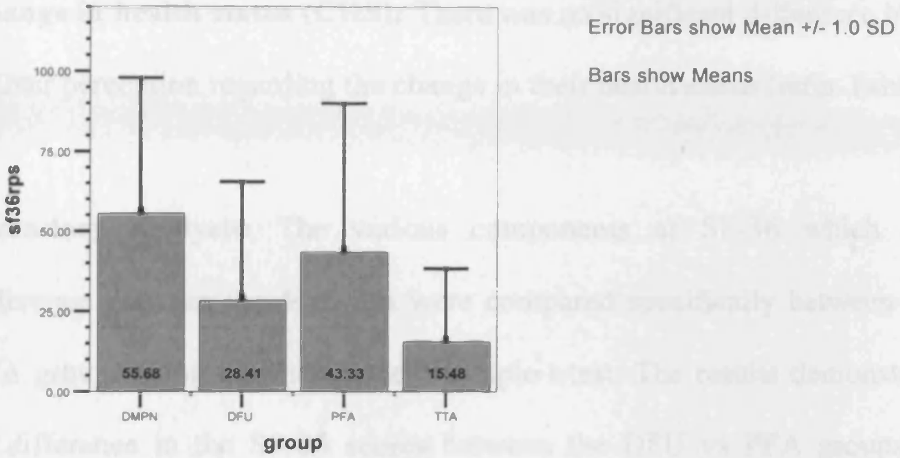
Descriptive comparison of the results from the present study with the healthy subjects demonstrated a decline in Social function from healthy subjects to diabetic patient groups indicated by a horizontal dotted line plotted in Figure 4.19.

Figure 4.19: Comparison of SF-36 Social function (sf36sfs) between the 4 groups



Role limitation due to physical problems (RPS): The 4 groups demonstrated significant differences in their role limitations due to physical problems (Table 4.29). The linear contrast between the 4 groups was significant demonstrating a decline in the score from the DMPN to DFU to TTA group. The DMPN group was affected the least whereas the TTA group was affected the most. However, the PFA group appeared to be less affected by physical problems compared to the DFU and the TTA groups (refer Figure 4.20).

Figure 4.20: Comparison of SF-36 Role limitation due to physical problems (sf36rps) between the 4 groups



Role limitation due to emotional problems (RES): There was no significant difference between the 4 groups in their role limitations due to emotional problems (refer Table 4.29).

Mental health (MH): The mental health score did not vary between the four groups (refer Table 4.29).

Energy / Vitality score (EVS): There was no significant difference between the 4 groups in their energy/vitality score (refer Table 4.29).

Bodily pain (PS): There was no significant difference between the 4 groups in their bodily pain score (refer Table 4.29).

General Health Perceptions (GHP): There was no significant difference between the 4 groups in their general health perception score (refer Table 4.29).

Change in health status (CHS): There was no significant difference between the 4 groups in their perception regarding the change in their health status (refer Table 4.29).

Secondary analysis: The various components of SF-36 which showed significant difference between the 4 groups were compared specifically between the DFU, PFA and TTA groups using the Independent sample t-test. The results demonstrated that there was no difference in the SF-36 scores between the DFU vs PFA groups and PFA vs TTA groups (refer Table 4.29).

Floor and ceiling effect: SF-36:

The two domains of SF-36 namely- the Physical Function and the Role limitation due to physical problems which showed significant declines from DMPN to TTA were examined for the possibility of the floor effect within the 4 groups separately to check whether the SF-36 score underestimated their performance in these two domains. The number of patients scoring below 20% within the 4 groups was noted.

It was interesting to note that there was a rise in the number of patients scoring less than 20% in the domains of Physical function and Role limitation due to physical problems from the DMPN to TTA group. The 4 groups demonstrated a consistent steady rise in the proportion of patients scoring below 20% in the Physical function domain (DMPN=3/23, DFU=4/23, PFA=5/23, TTA=10/23) with close to 50% of the patients in the TTA group. Such an observation indicates that with the progression of the physical impairment there was a greater possibility of the actual H-RQOL being worse than it was measured by the SF-36 in the aspect of Physical function especially in the TTA group. The domain of Role limitation due to physical problems also showed an overall decline from DMPN to TTA group indicating that with the progression of the physical impairment there was a greater possibility of the actual H-RQOL been worse than it was measured by the SF-36 in terms of Role limitation due to physical problems. However, it was interesting to note that there was greater number of patients with DFU compared to PFA suggesting that the Role limitation due to physical problems could have been actually worse than measured by SF-36 in patients with DFU compared to patients with PFA which matches well with the average score of the DFU group (28.41) compared to the PFA group (43.33) in this domain. Therefore, it can be inferred that the floor effect might not have allowed picking up the actual degree of clinical change across the 4 groups. Further investigation with larger sample size is necessary to repeat such a study to detect the actual degree of clinical change in H-RQOL of these patients especially in the domains of Physical function and Role limitation due to physical problems.

4.6B: Cardiff Wound Impact Scale (CWIS):

Primary analysis:

Well-being: The Well-being score was calculated only for the DFU group. Mean and S.D. of the well-being score are reported for the DFU group in Table 4.30.

Table 4.30: Mean and S.D. of CWIS Well-being score is reported for the DFU group

GROUP	DFU Mean (SD)
CWIS: W B (score)	36.69 (16.76)

CWIS: Physical Symptoms and Daily Living:

The four groups varied significantly in their Physical Symptoms and Daily Living (p=0.023) demonstrating a significant decline (refer Table 4.31) in the score across the four groups from DMPN to TTA (p=0.005).

Table 4.31: Comparison of CWIS Physical Symptoms and Daily Living score

Primary analyses						
Groups	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	ANOVA $F_{df,n}$	Linear polynomial contrast
CWIS PL (score)	78.99 (25.03)	65.33 (18.05)	66.02 (31.18)	56.16 (23.08)	$F_{3,81}$=3.366 p=0.023*	-25.483 – -4.839 p=0.005*

CWIS: Social Living

The four groups varied significantly in their Social Living (p=0.036). However no significant trend was observed across the four groups in their score (p=0.077) (refer Table 4.32).

Table 4.32: Comparison of CWIS Social Living score

Primary analyses						
Groups	**DMPN Mean (SD)**	**DFU Mean (SD)**	**PFA Mean (SD)**	**TTA Mean (SD)**	**ANOVA $F_{df,n}$**	**Linear polynomial contrast**
CWIS SL (score)	82.39 (26.74)	64.29 (23.30)	78.21 (22.61)	62.60 (28.16)	$F_{3,75}$=2.991 p=0.036*	-21.462 – 1.146 p=0.077

CWIS: H-RQOL:

The median and interquartile ranges (IQR) (25th to 75th percentile) for the 4 groups are presented in Table 4.33. The Kruskal Wallis test demonstrated no significant difference between the four groups (p =0.319).

Table 4.33: Comparison of CWIS H-RQOL across the four groups

Group	DMPN Median (IQR)	DFU Median (IQR)	PFA Median (IQR)	TTA Median (IQR)	Kruskal Wallis $Chi\text{-}square_{df}$ P value
CWIS: H-RQOL (score)	7 (6-8)	7 (4-8)	8 (5-9)	7 (5-7.25)	3.512_3 p =0.319

CWIS: Life satisfaction:

The median and interquartile range (IQR) (25^{th} to 75^{th} percentile) for the 4 groups are presented in Table 4.34. The Kruskal Wallis test demonstrated no significant difference between the four groups (p =0.358).

Table 4.34: Comparison of CWIS Life satisfaction across the four groups

Group	DMPN Median (IQR)	DFU Median (IQR)	PFA Median (IQR)	TTA Median (IQR)	Kruskal Wallis $Chi\text{-}square_{df}$ p value
CWIS: Life satisfaction (score)	7 (5-8)	7 (5-9)	8 (6-10)	6 (4.75-8)	3.229_3 p =0.358

Secondary analysis: The Physical Symptoms and Daily Living and Social Living scores were compared using the Independent sample t-test (refer Table 4.35). There were no significant differences in the domains of Physical Symptoms and Daily Living and Social Living of CWIS between the 3 groups (refer Table 4.35). Non-significant results between the 4 groups for the domain of H-RQOL and Life satisfaction (refer Tables 4.33 and 4.34) did not allow further specific group comparison.

Table 4.35: Comparison of the physical and social living scores within the CWIS

Secondary analyses					
Groups	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)	DFU vs PFA t_{df} p value	PFA vs TTA t_{df} p value
CWIS PL (score)	65.33 (18.05)	66.02 (31.18)	56.16 (23.08)	$-0.079_{22.536}$ p=0.938	$1.070_{26.348}$ p=0.294
CWIS SL (score)	64.29 (23.30)	78.21 (22.61)	62.60 (28.16)	$-1.724_{26.180}$ p=0.096	$1.756_{29.474}$ p=0.090

Standard Bonferroni correction was applied to adjust the significance level to p≤ 0.025.

4.7: Summary of results with respect to hypothesis testing:

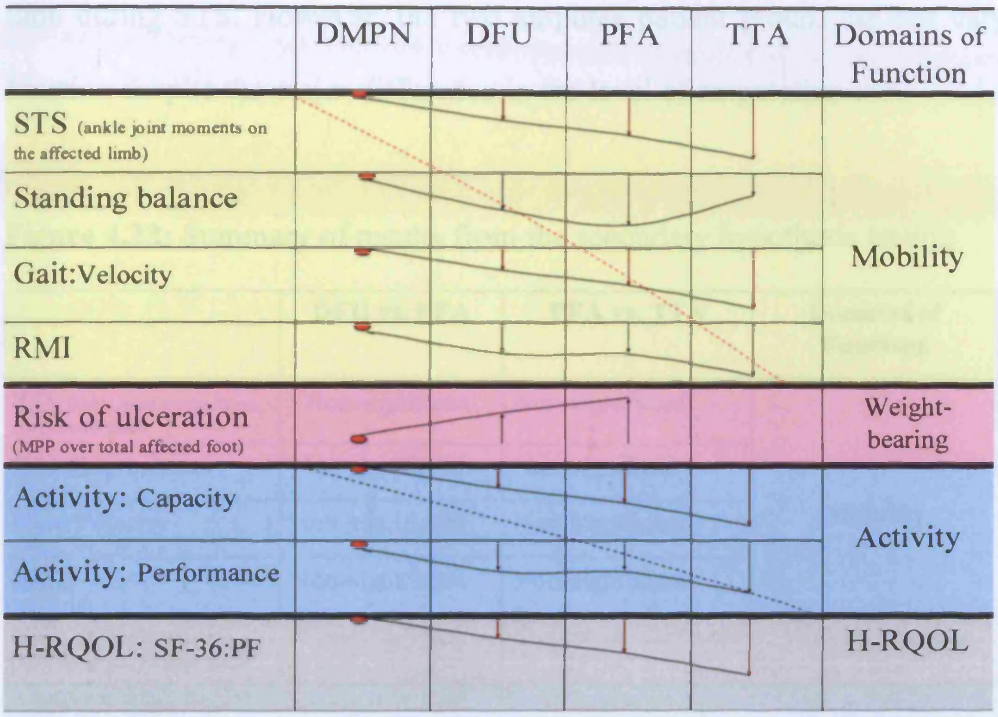
4.7A: Primary hypothesis:

The findings of the present study demonstrate that there was a significant difference in the functional outcome between the four groups i.e. DMPN, DFU, PFA and TTA. The four groups demonstrated an overall decline in the level of functional outcome with the progression of impairment resulting from consequent stages of foot complications in diabetic neuropathic people. All the three domains namely Mobility, Activity and H-RQOL demonstrated an overall decline from DMPN to DFU to PFA to TTA (refer Figure 4.21). The risk of plantar tissue injury to the entire affected foot as a result of the commonly performed weight-bearing task of mobility i.e. walking increased from DMPN to DFU to PFA group.

The dotted lines (red and blue) in Figure 4.21 represent the overall trend in the respective domain (mobility and activity respectively) and are not based on original data.

However, the individual components of the domain of mobility presented with slight variations in the pattern of decline. The four groups demonstrated a steady decline in their performance of STS task and gait; whereas the trend in standing balance and RMI varied. It was interesting to note that the balance of the TTA group in standing appeared to be better than the patients with PFA and DFU. Furthermore, the self-reported measure of mobility revealed a similar score in the DFU and PFA groups.

Figure 4.21: Summary of results from the primary hypothesis testing



4.7B: Secondary hypothesis:

It was interesting to investigate whether the two foot conditions i.e. DFU & PFA varied in the severity of their impact on the functional outcome of diabetic neuropathic patients.

The findings demonstrate that there was no significant difference in the overall function of the DFU and PFA groups (refer Figure 4.22).

Comparison between PFA and TTA groups revealed that the two groups did not show a significant difference in the overall function except in the domain of activity performance wherein the TTA group presented with low average daily walking performance compared to the PFA group.

Additionally the TTA group demonstrated low net knee and hip joint moments on the affected limb with a compensatory rise in ankle and hip joint moments on the contra-lateral limb during STS. However, the two amputee patient groups did not vary in their overall function despite the major difference in the level of amputation.

Figure 4.22: Summary of results from the secondary hypothesis testing

	DFU vs. PFA	PFA vs. TTA	Domains of Function
STS (ankle joint moments on the affected limb)	Non-significant	Non-significant	Mobility
Standing balance	Non-significant	Non-significant	
Gait: Velocity	Non-significant	Non-significant	
RMI	Non-significant	Non-significant	
Risk of ulceration (MPP over total affected foot)	Non-significant	Cannot be compared	Weight-bearing
Activity: Capacity	Non-significant	Non-significant	Activity
Activity: Performance	Non-significant	Significantly less	
H-RQOL: SF-36:PF	Non-significant	Non-significant	H-RQOL

Activity performance: The TTA group walked significantly less compared to the PFA group

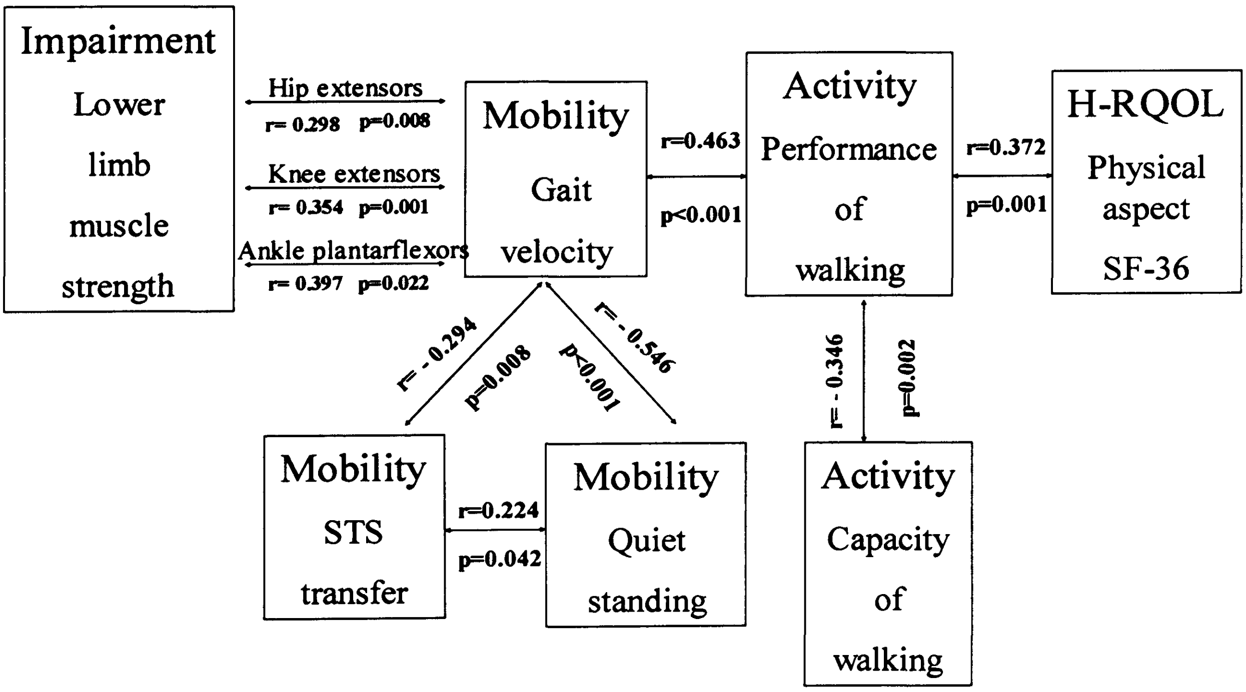
Section 2: Results from exploratory analyses:

Exploratory analyses were divided into two subsections. Subsection 1 presents the results from the exploration of the association between 3 domains of function. Whereas Subsection 2 presents the results from further exploration of the plantar pressures (MPP) walking within the DFU and PFA groups based on the location of the ulcer and the type of amputation and daily walking performance.

Subsection 1: Association between three domains of function

In addition to the hypotheses testing which involved the evaluation of differences in functional outcome of the four groups of patients at consequent stages of diabetic foot complications, the association between the 3 domains of function was explored. Before presenting the correlation findings between the 3 domains, the association between the 3 tasks of mobility and the correlation between mobility and impairment are presented in Figure 4.23.

Figure 4.23: Association between impairment, mobility, activity and H-RQOL domains of the proposed model for evaluation of functional outcome



Positive correlation between lower limb muscle strength and gait velocity indicates an association between impairment and mobility (refer Figure 4.23). Although positive the strength of the correlation between the 3 muscle groups and the gait velocity goes on decreasing from ankle plantarflexors (r=0.397) to knee extensors (r=0.354) to hip extensors (r=0.298).

The correlation findings demonstrate that the 3 tasks of mobility i.e. STS transfer, standing balance and gait were associated with each other. Negative correlation between the time taken to complete the STS transfer and the gait velocity (r= -0.294, p=0.008) indicates that lesser the time taken to complete the STS task faster is the gait velocity i.e. quicker the patient is in completing the STS transfer faster the patient is in walking. Greater value of time taken to complete the STS task indicates slower movement whereas greater value of gait velocity indicates faster movement.

Significant negative correlation between gait velocity and the COP excursion (r= - 0.546; p<0.001) indicates that better the stability in standing position greater is the gait velocity because higher values of COP excursion indicate greater instability.

Although weak, significant positive correlation between the COP excursion and the time taken for STS transfer reveals that faster the STS transfer better is the stability in standing position (r=0.224, p=0.042).

Results from analysis of correlation between gait velocity and average daily walking and average daily walking and physical function scored by SF-36 indicate a direct association between mobility and performance of activity and performance of activity and physical aspect of H-RQOL (refer Figure 4.23). Positive correlation between gait velocity and average daily walking indicated a direct relationship between the two variables. Although only 21% variance (R^2) was explained the significant correlation (r=0.463, p<0.001) between the two variables indicates that the decline in gait velocity is associated with a decline in the average daily walking of the patients. Also a positive correlation (r=0.372, p=0.001) between the average daily walking and the physical aspect of H-RQOL indicated a direct relationship between these two variables (14% variance explained).

Significant negative correlation between the capacity and performance of walking indicates that higher the energy expenditure less is the average daily walking (r=-0.346, p=0.002) establishing the association between capacity and performance of walking.

Summary of results from exploratory analyses:

The results from the exploratory analyses confirm the association between the 3 domains of function namely: mobility, level of activity and physical aspect of H-RQOL. Moreover, the three outcome measures representing the three tasks of mobility i.e. STS transfer, standing balance and gait velocity were associated with each other and mobility was related to impairment of lower limb muscle strength.

Between the impairment and task of mobility, the lower limb muscle strength (hip extensors, knee extensors, ankle plantarflexors) was directly associated with the gait velocity.

Within the domain of mobility the time taken to complete the STS transfer was inversely related to the gait velocity i.e. longer the time the patients took to complete the task slower they walked. Balance in standing and the gait velocity also demonstrated a negative relation indicating that greater the instability in standing slower was the speed of walking. The speed of the STS transfer was directly associated with the stability in standing position. Between the 3 domains a decline in gait velocity was directly related to a decline in the daily walking performance. A decline in the daily walking activity was directly related to a decline in the physical aspect of H-RQOL.

Subsection 2: Further exploration of plantar pressures within DFU & PFA groups

The DFU and PFA groups included patients with different locations of plantar ulcers and different types of PFA respectively. It was reasonable to expect that both these factors would affect the regional pressures (MPP) over the foot. Therefore, further exploration of the plantar pressures was conducted within these two groups.

The DFU group of the present study included patients with varied locations of plantar ulceration (toe=3, 1-2 metatarso-phalangeal region=7, 3-5 metatarso-phalangeal region=6, hallux=2 and heel=5). Therefore although the majority of patients had fore-foot ulceration (n=18), the averaging effect of various sites of ulcers probably will have masked the otherwise pronounced peak pressures over the fore-foot. In order to demonstrate the possibility of the averaging effect the DFU group patients were further classified into 2 subgroups based on the site of ulceration. The higher average MPP values of the DFU subgroup with fore-foot ulceration (n=18) compared to the average MPP of the total DFU group (n=23) and the lower average MPP values of the DFU subgroup with heel ulceration (n=5) compared to the average MPP of the total DFU group (n=23), explains the likely effect of averaging of the peak pressures due to different ulcer locations (refer Table 4.36).

Table 4.36: MPP in subgroups within the DFU group classified based on site of ulceration

Plantar areas	DMPN group n=23 Mean (S.D.)	Total DFU group n=23 Mean (S.D.)	DFU group with forefoot ulceration n=18 Mean (S.D.)	DFU group with heel ulceration n=5 Mean (S.D.)
Total foot area (kPa)	356.4 (88.9)	359.2 (70.8)	369.8 (62.3)	325.4 (92.8)
1-2 MTP (kPa)	332.7 (103.2)	**324.6** (116.7)	**356.5** (66.9)	**222.5** (184.8)
3-5 MTP (kPa)	279.1 (89.2)	264.7 (101.2)	286.2 (76.1)	195.8 (147.3)
Heel (kPa)	251.8 (39.5)	215.5 (72.2)	228.8 (60.0)	173.1 (97.9)

Similarly further classification of the PFA group into subgroups based on the level of PFA demonstrated the discrepancy in the midfoot pressures caused by the level of PFA (refer Table 4.37). It needs to be highlighted that the average midfoot pressures were highest in the patients with TMA amputations followed by those with hallux amputation and with hallux and toe amputations since loss of the forefoot either completely (TMA) or partially (hallux or hallux with toes). Whereas the patients with ray amputations presented a picture similar to the DMPN group in terms of the average pressures over the midfoot.

Table 4.37: MPP in subgroups within the PFA group classified based on level of PFA

Plantar areas	DMPN group n=23 Mean (S.D.)	Total PFA group n=16 Mean (S.D.)	PFA group with TMA n=5 Mean (S.D.)	PFA group with Hallux amputation n=4 Mean (S.D.)	PFA group with Hallux + toe amputation n=2 Mean (S.D.)	PFA group with Ray amputation n=5 Mean (S.D.)
Total foot area (kPa)	356.4 (88.9)	400.3 (108.0)	425.0 (77.5)	415.6 (68.0)	306.4 (119.8)	401.0 (158.9)
Midfoot (kPa)	82.9 (41.1)	**184.2** (177.8)	**384.1** (157.2)	128.6 (136.5)	130.6 (98.2)	50.4 (22.2)

Secondly, it was expected that the daily walking performance of the DFU group patients might be influenced by the instructions the patients received regarding the volume of walking during the period of wound healing. Therefore descriptive analysis of the average daily strides of the subgroups classified as per the walking instruction was performed (refer Table 4.38).

Table 4.38: Subgroups of DFU group patients classified based on received walking instruction

	Total DFU group n=23 Mean (S.D.)	No. of patients instructed to walk for ADL n=12 Mean (S.D.)	No. of patients received no walking instructions n=8 Mean (S.D.)	No. of patients instructed not to walk at all n=2 Mean (S.D.)	No. of patients who received dual instructions: no walking at all & walk for ADL n=1
Average daily strides	3058 (1994)	2538 (1594)	3554 (2382)	5244 (2785)	1965

The patients who were instructed to walk only as much as necessary for daily activities actually walked less (1016 strides less) compared to patients who received no instructions regarding the walking activity. Also the average value of the total DFU group (n=23) was close to the average value of the sub group of patients who received no instructions regarding their walking activity. The patients who were instructed to offload the foot completely walked almost twice the number of daily strides (5244) compared to the patients who were instructed to walk only as much as needed for ADL (2538).

Chapter 5: Discussion

The objective of this study was to explore functional outcome in patients with diabetic neuropathy at four consequent stages of foot complications namely diabetic neuropathy, plantar ulceration, partial foot amputations and trans-tibial amputations. The primary objective was:

1. To investigate the nature of the course of functional outcome across the four groups.

The secondary objectives were:

1. To compare the functional outcome between the DFU group and the PFA group.
2. To compare the functional outcome between the PFA and the TTA group.

Prior to the discussion of the results of this study, the key-features of the patient characteristics of the study cohort are summarised. Specific characteristics are mentioned in the discussion of the results of the relevant outcome measures.

5.1: Subject characteristics of the four groups: age, gender, type of DM, duration of DM

5.1A: Demographic features:

All the 4 groups were matched on marginal distributions for age, height, body mass and body mass index. However, the distribution of the subjects in terms of gender, type of DM and duration of DM is not exactly equal. There was a consistent over-representation of males in all the four groups. Previous studies in diabetic neuropathic patients have also documented such a pattern (Sorensen, Molyneaux & Yue 2002). The distribution of male: female in various reports studying diabetic neuropathic patients is presented in Table 5.1, which demonstrates greater number of males compared to females among patients with DMPN. Therefore in the background of the previous reports, the over representation of males in the present study appears to represent a general pattern of DMPN. However, it is unknown whether there is any specific metabolic milieu associated with male gender (Sorensen, Molyneaux & Yue 2002).

Table 5.1: Data from previous studies demonstrating the over –representation of males among patients with DMPN

Total no. of subjects with DMPN	Ratio= Male:female	Total % of male subjects	Reference
34	20:14	59	D'Ambrogi et al. 2005
10	8:2	80	Armstrong DG et al. 1999
17	13:4	76	Simoneau GG et al. 1996
345	218:127	63	Vishwanathan V et al. 2003

5.1B: Type of DM:

Overall, there were a higher number of patients with Type 2 DM than Type 1 DM in the total sample. The DFU, PFA and TTA groups consistently showed a greater number of patients with Type 2 DM compared to Type 1 DM except the DMPN group, which showed a greater number of patients with Type 1 DM compared to Type 2 DM. Although it would have been ideal to match the groups on the type of DM, it was difficult to recruit all the 4 groups of patients with only Type 1 or Type 2 DM. However, it would be interesting to explore the association between the type of DM and functional outcome of diabetic neuropathic patients at different stages of foot complications with future studies.

5.1C: Duration of DM:

It is believed that the prevalence of DMPN increases with the duration of DM (Scheen 1998). Similarly, it can be argued that the duration of DM is associated with the progression of foot complications and ultimately if it can have an impact on the functional outcome of diabetic neuropathic patients at various stages of foot complications is unclear. Although the present study does not answer this question it may be reasonable to expect that the duration of DM may be directly associated with the progression of foot complications. However, it is hard to imagine the nature of association (if any) between duration of DM and functional outcome of patients with foot complications. Even if further research establishes an association between the duration of DM and the progression of foot complications, duration of the disease may appear to be one of the many general systemic factors in DM, which operate in the background without demonstrating a directly evident influence on the functional activities of the diabetic neuropathic patient. It would be difficult to investigate the solitary influence of the duration of DM on the functional outcome of this patient group.

Moreover, in the present study the information relating to the duration of DM relied totally on the patient's memory because it was difficult to trace the actual medical records to find out when the patient was diagnosed with DM. Most patients reported that DM was diagnosed when they were investigated for other health problems, making the information less reliable for analysis. In addition, there is evidence to suggest that the duration of DM and the type of DM is not related to the risk of foot ulceration (Boyko, Ahroni, Stensel, Forsberg, Davignon & Smith 1999). Therefore, no further analysis was conducted with respect to the duration of DM in the present study.

5.1D: Wound location and type of PFA (DFU and PFA group):

The DFU and the PFA groups were heterogeneous in terms of the site of plantar ulceration and the level of foot amputation. The DFU group included patients with a mixture of location of plantar ulceration (toe=3, MTP 1-2=7, MTP 3-5=6, hallux=2 and heel=5). Similarly, various types of foot amputations (hallux=4, hallux+toes=2, ray=5 and trans-metatarsal=5) were collectively classified as PFA for this study. Such a heterogenous presentation of these 2 groups made it difficult to interpret the plantar pressure distribution in terms of specific plantar areas at risk of injury. On one hand, such a presentation can be considered as a limitation of the present study whereas on the other hand it represents the general clinical scenario.

5.1E: Foot deformities:

Foot deformities are observed in 66% of patients with DM (Vermigli, Carrington & Boulton 1996) and they include callus, hallux valgus, claw toe, hammer toe, Charcot osteo-arthropathy, forefoot varus and valgus. Although deformity of the foot has been recognised as a factor in elevating plantar pressures in diabetic neuropathic foot (Boyko, Ahroni, Stensel, Forsberg, Davignon & Smith 1999) it would be near impossible to recruit patients of all the four groups with similar foot shape considering the prevalence of foot deformities in this patient group. However having recruited patients who presented with a mixture of such foot deformities it can be criticised, whether the foot deformities were measured and their impact on plantar pressures was studied.

Concurrently it is acknowledged that accurate measurement of foot deformities requires techniques such as ultrasound, radiography, computed tomography and magnetic resonance imaging (Bus 2004). Clinical measurements of the foot shape using surface markers may not be accurate because the soft tissue on the plantar surface of the foot is thick and variable and can mask the true bony architecture of the foot (Williams & McClay 2000). Furthermore, the presence of the swelling around the ankle and foot observed in some of these patients would make the findings further inaccurate. Therefore, the findings may not indicate the actual skeletal deformities.

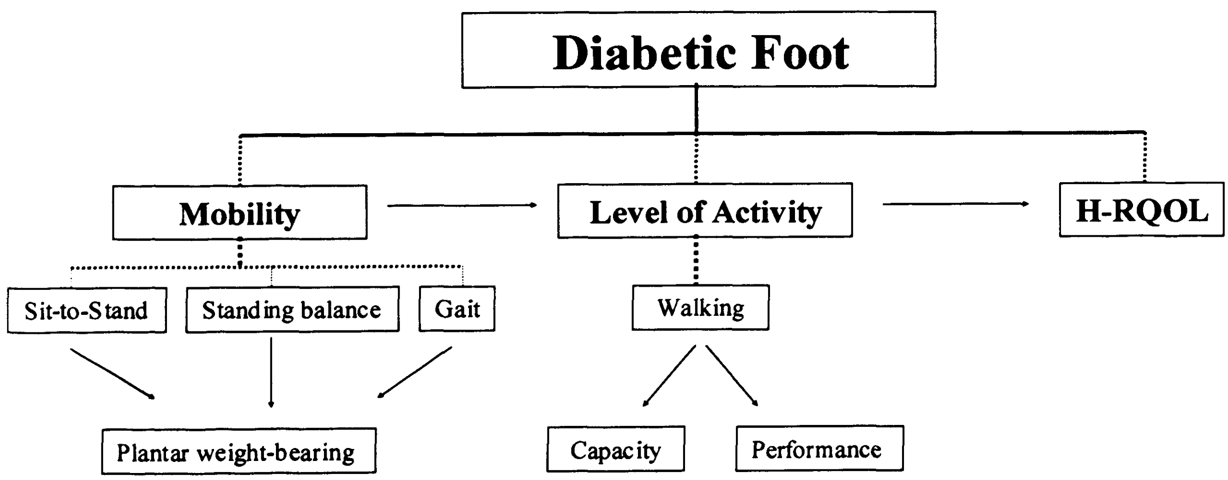
Furthermore, the focus of this study was not to compare the functional outcome in diabetic neuropathic patients with different types of foot deformities. Therefore the foot deformities were not quantified but it was confirmed with visual inspection of medial-lateral photographs of the feet (Cowan, Jones & Robinson 1993) that no patients presented with complete obliteration of the medial longitudinal arch of the foot as that might be expected to alter the forefoot plantar pressure distribution.

It was also confirmed that no patient with Charcot osteo-arthropathy was included in the study because Charcot foot is known to present with a collapsed arch (Hartemann-Heurtier, Ha Van & Grimaldi 2002) which can alter the pressure distribution over the forefoot. The dispersion of the foot deformities for e.g. hallux valgus, claw toe and cavus foot within the four groups appeared to be similar in the 4 patient groups (refer Table 4.9).

Therefore, the present study adopted a reasonably practical approach of identifying the alteration in the medial longitudinal arch to rule out the possibility of variation in the proportion of forefoot to hindfoot pressure distribution due to obliteration of the medial longitudinal arch of the foot. Moreover, it needs to be highlighted that no particular group was dominated by any specific foot deformity.

After discussing, the subject characteristics of the four groups the functional outcome is discussed based on the various domains described in the proposed model of function (refer Figure 5.1).

Figure 5.1: Proposed model of functional outcome



5.2: Impairment: Diabetic Neuropathy:

Loss of protective sensation from diabetic neuropathy was the impairment common to the patients belonging to all the four groups. However the score of neuropathy was significantly different between the 4 groups ($p=0.001$). Patients with DFU, PFA and TTA presented with more severe neuropathy compared to the controls. The unequal distribution of the neuropathy score across the four groups suggests that the severity of neuropathy increases with the progression of the diabetic foot disease. It is likely that the DMPN group of the present study represents the diabetic neuropathic population, which is at an early stage of foot complications compared to the remaining neuropathic groups with further foot complications. Therefore although it may appear ideal to match the 4 groups on their neuropathy score in the first instance, on reflection it might be purely hypothetical to attempt to match the four groups at consequent stages of foot complications on the severity of neuropathy due to several reasons.

It is already known that diabetic neuropathy is associated with diabetic foot disease at various stages of foot complications (Sima & Greene 1995, Frykberg, Harvey, Lavery, Harkless, Pham & Veves 1998). In that context, it may be likely that the severity of DMPN increases with the duration of DM although the association between the course of progression of the neuropathy and diabetic foot complications remains unexplored. Therefore, even if this study was conducted with an ideal study design (e.g. a longitudinal study) it is reasonable to expect that the diabetic neuropathic patient groups with consequent stages of foot complications present with more severe neuropathy compared to neuropathic group with no further foot complications. Peters et al. (2001) has reported a similar observation during an attempt to compare the functional status of diabetic patients with lower limb amputations compared to diabetic patients without amputations (Peters, Childs, Wunderlich, Harkless, Armstrong & Lavery 2001). The group of patients with amputations presented with more severe disease (high prevalence of peripheral vascular disease and neuropathy) than patients without amputations. The authors had a similar argument that, generally the patients requiring a lower extremity amputation have a longer duration of DM and therefore have developed more complications of this multi-system disease.

Moreover, it was difficult to recruit enough patients to be able to match the 4 groups based on the severity of neuropathy. Therefore, the unequal distribution of neuropathy status is accepted as a limitation of the study and the findings from the present study are interpreted accordingly. In addition, the likely influence of severity of neuropathy score on certain outcome measures of function is discussed in the respective sections of the chapter.

5.2A: Associated sensory assessment:

Assessment of presence of vibration sense in the present study demonstrated that 64.3% of patients with diabetic neuropathy (which was confirmed by loss of protective sensation detected by 5.07 S-W monofilament) showed loss of vibration perception. Whereas, 34.5% of patients with loss of protective sensation (detected by 5.07 S-W monofilament) showed an intact vibration perception. However there was no significant difference in the vibration perception sensation between the 4 groups (p=0.32). Marked inconsistencies within sensory modalities are already known. For example, the ability to perceive a cutaneous vibratory stimulus may be relatively well preserved while the cutaneous perception of touch/pressure is markedly reduced (Simoneau et al. 1996). Even Kastenbauer et al. (2004) have reported inconsistency between the findings from sensory testing performed by S-W monofilament and tunning fork. They reported that monofilament test was abnormal in 7.2% of diabetic patients with a normal vibration perception threshold (VPT) and abnormal in 66.7% of subjects with disturbed vibration sense (Kastenbauer et al. 2004).

Moreover, it needs to be highlighted that in the present study the vibration sensation was tested over the the medial aspect of the head of the 1st metatarsal [a study reporting the normative data for quantitative vibration testing in children, juveniles and adults has also tested the sensation at the second metacarpal bone and above the 1st metatarsal bone (Hilz et al. 1998)] unlike the previous researchers who tested the VPT over the tip of the great toe (Kastenbauer, Sauseng, Brath, Abrahamian & Irsigler 2004). It is likely to have a dampening effect of the vibratory stimulus if applied over the tip of the great toe because of the possibility of swelling of the foot and thereby less prominent bony prominence compared to the medial aspect of the head of the 1st metatarsal resulting in a greater proportion of people with disturbed vibration sense.

Based on the previous evidence, which demonstrates marked inconsistencies within sensory modalities and the similar findings from the present study, it needs to be emphasised that the objective of sensory testing in the present study was only to confirm the loss of protection sensation in clinically established cases of DMPN and not to quantify the sensory impairment with the purpose of monitoring it over time. Inability to feel the 5.07 monofilament is already established as a clinical measure of loss of protective sensation. Therefore, confirmation of the loss of protective sensation by 5.07 S-W monofilament was sufficient to confirm the presence of DMPN in diabetic patients who were clinically diagnosed cases of DMPN.

5.2B: Joint motion & Muscle strength:

Limited joint mobility and decreased muscle strength are known to be associated with diabetic peripheral neuropathy (Rozadilla, Montana, Nolla, Soler & Escofet 1991, Andersen, Gjerstad & Jakobsen 2004).

The findings of the present study demonstrate that there was no significant difference in the hip, knee and the ankle joint motion in the sagittal plane between the 4 diabetic neuropathic groups on the affected and the contra-lateral limb despite the progression of foot complications. However the 1st MTP-joint motion in the sagittal plane was significantly less (58%) in the DFU group compared to the DMPN group ($p<0.001$) on the affected foot. On the affected side, the MTP joint motion was compared only between the DMPN and DFU group as the data were not available for the PFA and TTA groups for obvious reasons. On the contra-lateral limb also the motion at the 1st MT-P joint was significantly different between the 4 groups ($p<0.001$) with the DFU group presenting with the lowest score.

On the affected foot, the reduction in the MTP joint motion is not surprising in the presence of the likelihood of inflammatory reactions in the foot associated with active plantar ulceration. No studies were located to compare the 1st MTP joint motion in patients with active ulceration. However Delbridge et al. (1988) have also confirmed that the diabetic patients with history of foot ulceration demonstrate greatest impairment of the joint mobility compared to diabetic patients with no history of foot complications and non-diabetic controls based on their findings from subtalar joint motion (Delbridge et al. 1988). Moreover, there are reports, which have documented the ROM at the 1st MTP joint in diabetic neuropathic patients at various other stages of foot complications (Duffin et al. 1999, Viswanathan et al. 2003). Duffin et al. (1999) reported 66° of extension motion at the 1st MTP joint in 302 Type 1 diabetic adolescents measured with an orthopaedic evaluation device in the weight-bearing position. However, Viswanathan et al. (2003) reported 53.3° (flexion=33.4°, extension=19.9°) in 110 diabetic neuropathic patients and 44.5° (flexion=28.1°, extension=16.4°) in 85 diabetic neuropathic patients with history of ulceration measured with a goniometer in the supine position. The normal ROM at the 1st MTP joint is approximately 50-60° extension and 30-40° flexion i.e. a total range of 80-100° in the sagittal plane (Kapandji 1987).

The present study reported 69° of motion at the 1st MTP joint in the sagittal plane (flexion and extension) in a supine position measured with the video analysis (siliconCOACH software) in DMPN patients whereas 29° (combined range of motion of flexion and extension) in diabetic neuropathic patients with active plantar ulceration. The variations in the degree of motion between studies can be attributed to the different stages of foot complications and the difference in methodology. However, it is evident that the mobility at the 1st MTP motion decreases significantly following foot ulceration in diabetic neuropathic patients and can be identified as a potential risk factor in the development of further foot ulceration.

On the contra-lateral foot, the reduction in the 1st MTP joint motion can be attributed to changes that occur in the collagen system due to DM superimposed by the likely mechanical changes occurring in the musculo-skeletal system following further foot complications such as DFU (36°), PFA (41°) and TTA (45°). The lowest score of the DFU group even on the contra-lateral foot could result from the restricted ambulant mobility (prolonged period of immobilization) of these patients during the phase of ulcer healing. It is not clear why the 1st MTP joint is affected the most. This might be the case because it is the most mobile joint of the foot (because of which the reduction in mobility becomes evident) and forms an integral part of the foot complex within which the maximal changes occur in the vascular, neural, collagenous and musculo-skeletal systems due to DM. Another reason could be that researchers in the past have focussed their attention on changes occurring in the ankle-foot complex due to DM. There is very little evidence to indicate that changes occurring in the more proximal joints of the lower extremity such as the hip and the knee are due to DM. Therefore, it was difficult to compare the findings of the present study with previous reports.

The minimal reduction in the joint motion at the hip joint (DMPN=96°, DFU=96°, PFA=103°, TTA=97°) compared to the normative data (age group 60-74 yrs, 118°) can be attributed to changes occurring due to advancing age (Roach & Miles 1991) (the mean age of the participants in the present study was 62.8 yr). The knee joint motion in flexion in the present study (DMPN group=131°) was similar to the findings reported by Roach & Miles (1991) in the same subject cohort (131°) mentioned above.

However, limited joint mobility of the feet and the hands is not surprising since it is well established in diabetic patients (Carvallo et al. 1991, Rozadilla, Montana, Nolla, Soler & Escofet 1991, Garg et al. 1992, Fernando & Vernidharan 1997, Simmons, Richardson & Deutsch 1997). In addition, the correlation between limited mobility of the foot and the rise in peak plantar pressures is already established in diabetic patients (Mueller et al. 1989, Fernando et al. 1991, Payne, Turner & Miller 2002). In univariate studies, the syndrome of limited joint mobility of the foot has been correlated with increased plantar pressure (Fernando, Masson, Veves & Boulton 1991). Whereas in multi-variate studies, the range of motion was only correlated to hallux pressures (Payne, Turner & Miller 2002). In the light of this previous evidence the likely influence of impaired joint mobility in the alteration of peak pressures cannot be over looked. However, the focus of this study was not to evaluate the effects of DMPN and its further foot complications on the joint mobility and muscle strength, which have been already established. Therefore, joint ROM and muscle strength were evaluated in the present study only to rule out any gross muscle weakness (gross impairment in muscle strength was defined as inability to complete the full range of joint motion actively) or movement restriction resulting from neuro-musculo-skeletal system disorders apart from diabetic neuropathy, which would influence the interpretation of biomechanical variables of the study.

Comparison of the average scores of the muscles around the hip (flexors, extensors, abductors and adductors), knee (flexors and extensors) and ankle (dorsiflexors and plantar flexors) indicates that there was a fairly equal dispersion of the hip muscle strength scores between the four groups. The strength of the knee flexors (28% less than DMPN) and extensors (29% less than DMPN) on the affected limb was significantly different between the four groups (p=0.013 & p=0.039 respectively) with the TTA group demonstrating the least average group scores. The strength of the ankle dorsiflexors (24% less than DMPN) and plantar flexors (27% less than DMPN) on the contra-lateral limb varied significantly between the 4 groups (p=0.028 & p=0.039 respectively) with the TTA group demonstrating the least average group scores.

The average values of knee extensors and flexors of the DMPN group in the present study (30.17 & 17.3 kg force respectively) were close to the average values of knee extensors and flexors (23.9 & 13.0 kg force respectively) measured by Lord et al. (2005) in older subjects (75 yr and above) who were at risk of falling due to unknown causes. The slightly higher average values in the present study can be explained by the younger age group (65.5 yr) of participants with DMPN alone as muscle strength is known to decrease with advancing age (Marcus 1995).

To summarise, the difference within the groups was possibly due to the low muscle strength of the amputated limb and the contra-lateral limb of the TTA group. The decreased strength of the muscles around the knee may be due to the mechanical disadvantage caused by the TTA due to a short lever arm. The decreased strength of the muscles around the ankle in the TTA group could be partially an effect of DMPN (TTA group apparently presented with severe neuropathy). The reduction in ankle muscle strength could be partially due to the deconditioning effect caused by the likely prolonged periods of immobilisation during the sequelae of events, which generally lead to a major amputation following diabetic neuropathy, such as foot ulceration and probably a PFA. Although such an observation (reduced lower limb muscle strength of the TTA group) does not add to the existing body of knowledge these findings are considered in the interpretation of the results of joint moments during STS task and gait because of the known influence of muscle force on joint moments (Andriacchi et al. 1980).

To summarize the findings from the impairments of all 4 groups, diabetic neuropathy was common to the entire patient cohort. The DFU, PFA and TTA groups appeared to present with more severe neuropathy compared to the DMPN group, which may resemble the general clinical scenario among patients with DMPN. However, the unequal distribution of the neuropathy status between the 4 groups is treated as a limitation of the study and the findings are interpreted accordingly by investigating the likely influence of neuropathy on the outcome measures.

All four groups were investigated to rule out the presence of Charcot osteoarthopathy, which involves major musculo-skeletal changes in the foot, which could effectively influence the performance of the foot in the weight-bearing activites such STS, gait and the total volume of daily walking. However, the similar dispersion of the commonly encountered diabetic foot deformities such as hallux valgus, cavus foot and claw toes was confirmed.

In terms of joint mobility, the DFU, PFA and TTA groups appear to present with decreased joint range of motion at the 1st MTP joint with the DFU group demonstrating the lowest score compared to the remaining groups. This observation was considered in the interpretation of the plantar pressure distribution during walking.

Assessment of lower limb muscle strength revealed that the TTA group demonstrated the least strength on the amputated and the contra-lateral limb compared to the remaining 3 groups. This finding was considered in the interpretation of the results of STS and walking activity.

Although the results from the various impairments do not add to the existing body of knowledge it needs to be highlighted that the impairments of the patients were considered in the interpretation of the outcome measures used to assess their functional outcome.

5.3: Mobility:

5.3A: Sit-to-stand movement:

Rising from a chair is the cornerstone of ambulant mobility since it is a pre-requisite for standing and walking. Assessment of sit-to-stand movement is one of the important functional evaluations that physical therapists carry out when caring for patients with neurological or lower extremity dysfunction (Jeng et al. 1990). The importance of the movement has fascinated researchers to study the mechanics of sit-to-stand in people with various disorders affecting their mobility for e.g. stroke, rheumatoid arthritis, paraplegia, knee arthroplasty, low back pain, Parkinson's disease, cerebral palsy etc. (Berger, Riley, Mann & Hodge 1988, Gioftsos & Grieve 1996, Munro et al. 1998, Kamnik, Bajd & Kralj 1999, Brunt et al. 2002, Cheng, Chen, Wang & Hong 2004, Hennington, Johnson, Penrose, Barr, McMulkin & Van der Linden 2004, Inkster & Eng 2004) .

Although DM is one of the common chronic disorders of the elderly population resulting in substantial morbidity following foot complications the mechanics of sit-to-stand transfer in this population is least understood. The focus of STS analyses in this study was to evaluate the impact of various diabetic foot complications on the performance of the movement, in terms of i) time taken to complete the task, ii) time taken to attain stability following completion of the STS task, iii) lower extremity net joint moments and iv) asymmetry in STS performance in the presence of unilateral diabetic foot disease (DFU/PFA/TTA).

There was no significant difference in the time taken to complete the STS task at their natural pace although the 4 groups represented progressive stages of foot complications. The average values of the 4 groups i.e. DMPN (1.5 s), DFU (1.6 s), PFA (1.6 s) and TTA (1.9 s) may demonstrate that there was a very slow rise in the the total time required for completion of the task but the difference was non-significant (p=0.209) possibly due to the poor sensitivity of this outcome measure. However, the non-significant difference between the groups allowed comparing the actual values of the net joint moments without accounting for the speed of the movement because the speed of the movement is likely to have an influence on the muscle forces produced. The time taken to complete the STS task (which was defined as the point of full extension of the body) by the DMPN group was similar to the time reported by Pai & Rogers (1991) in their study describing the STS movement of 8 healthy volunteers (26-38 yrs) at their natural pace.

The time taken to stabilise after the completion of the STS task did not vary between the 4 groups (p=0.201) although the average group values demonstrated that the DMPN group (6.8 s) took the least time whereas the DFU group (9.1 s) took the maximum time to attain stability. The time taken to attain the stability can be considered as a measure of dynamic stability and therefore it is interesting to note that although the 4 groups varied significantly in their static stability (i.e. stability in standing position. COP excursion in meter was considered as the measure of static stability. Refer to the discussion on Quiet standing in section 5.3B) they did not differ in their dynamic stability.

The notable features of this study include findings related to the influence of unilateral diabetic foot disease for e.g. plantar ulceration, partial foot amputation and trans-tibial amputation on the affected and contra-lateral limb during the STS movement.

The key finding was the asymmetry in net joint moments resulting in relatively larger moments on the contra-lateral limb. Of all the 4 groups, the TTA group was affected the most followed by the DFU group. The asymmetry during rising from sitting was confirmed by the majority (86.4%) of TTA group patients (n=19/22=86.4%) and more than half

(56.5%) of the DFU group patients (n=13/23=56.5%) bearing weight through the contra-lateral limb. However, the patients of the DMPN group in the present study presented with a similar pattern of weight distribution as normal subjects demonstrating a virtually symmetrical distribution of weight during STS (Engardt & Olsson 1992).

On the contra-lateral side, the TTA group compensated with larger joint moments of the ankle and the hip (increase of 50.85% in the hip moments compared to the DMPN group). Only one previous study which studied the STS movement in a patient with TTA in a group of patients with varied disabilities reported that the patient (age=67 yr) with high left TTA had to exert a much higher knee moment on the right compared to normal (Burdett et al. 1985). The present study demonstrated that the affected knee moment was least in the TTA group (30% less compared to the DMPN group). However, knee moments on the contra-lateral limb did not vary significantly between the four groups suggesting that the patients with unilateral foot complications, especially the TTA group relied on the contra-lateral hip and the ankle for compensatory support to complete the task rather than the knee joint.

A person with normal neuro-muscular control tends to use a movement pattern, which ensures relatively small joint torques in order to reduce the necessary muscle force and thereby reduce energy expenditure (Doorenbosch et al. 1994). Nevertheless, transferring from a sitting to a standing position requires large torques, particularly at the hip and the knee (Kelley, Dainis & Wood 1976, Fleckenstein et al. 1988, Rodosky, Andriacchi & Andersson 1989, Pai & Rogers 1991, Roebroeck et al. 1994). Results of the present study are in agreement with these reports demonstrating that the net joint moments during the total movement were greatest at the hip followed by the knee and the ankle. Although it was difficult to compare absolute values of net joint moments from the present study with previous reports due to the differences in the methodology, it needs to be noted that the pattern of the joint moments of the lower extremity was similar.

After analysing the impact of unilateral foot complications secondary to DMPN on the lower limb joints, the symmetry of STS performance was analysed. It may appear in the first instance that the information gathered from this analysis may not be directly related to the functional outcome of the diabetic neuropathic patients. However, it was deemed necessary to investigate the symmetry of the STS task of these patients in the presence of unilateral foot complications such as DFU, PFA and TTA in terms of the risk of plantar injury during a repetitive daily weight-bearing task such as STS transfer.

Unilateral LEAs are likely to cause asymmetry in weight-bearing movements involving both limbs. While analysing gait Winter and Sienko (1988) stated that any human system with major structural asymmetries in the neuro-muscular system cannot be optimal when the gait is symmetrical. In the similar context, it would be hard to expect the patients with unilateral TTA to rise from a chair symmetrically. Patients with unilateral TTA compensated with increased joint moments of the ankle and the hip on the contra-lateral limb to rise from the chair successfully. The increased participation of the contra-lateral limb was confirmed by the majority of patients of the TTA group (n=19/22 i.e. 86.4%) demonstrating increased weight-bearing on the contra-lateral limb during rising from the chair. Hemiplegic subjects with unilateral neuro-muscular disorder are also known to demonstrate a similar asymmetry with increased weight-bearing through the unaffected leg during STS (Engardt & Olsson 1992, Durward 1994). The authors presumed that the marked asymmetry in the distribution of weight-bearing could be associated with the marked asymmetrical movement pattern although this has not been established. It is not clear whether the kinetic asymmetry (weight-bearing force) can be associated with kinematic asymmetry of a particular movement.

The kinematics of the STS movement were not evaluated in the present study to describe the pattern of the movement however the results from the net joint moments of the lower limb link with the weight-bearing distribution of the TTA group during the STS task. The significantly higher hip and ankle joint moments on the contra-lateral limb of the TTA group can clearly explain the increased weight-bearing on the contra-lateral limb.
Revisiting the normal mechanics of the STS task can help to understand the need of the TTA group to rely on the contra-lateral limb for the successful completion of the movement. Normally in STS transfer, the most marked joint rotations occur in the hip and knee joints. Both the joints extend along with plantar flexion of the ankle from seat-off to the end of the movement to control the direction of GRF (after seat-off the GRF points in front of the hip and ankle joint and passes far behind the knee) necessary to maintain the postural balance (Roebroeck et al. 1994). Therefore, it seems reasonable to expect that the lack of ability of the prosthetic ankle-foot complex to hinge the distal end of the system, the decreased muscle strength noted in the knee extensors on the affected limb of the TTA group (refer to Table 4.8) and the absence of sensory feedback from the prosthetic foot, required the amputee group to transfer the weight on the contra-lateral foot and rely more on the contra-lateral limb to complete the movement safely.

Moreover it was noted that the TTA group used only 76.5% of their strength of the knee extensors during STS (Maximal muscle strength) resulting in low knee moments on the affected limb. This observation can be explained by the mechanical inefficiency of the prosthetic lower limb to hinge the prosthetic ankle-foot complex effectively and utilise the maximal available knee extensor strength to extend the knee. Participants appeared to compensate with their contra-lateral hip by using their hip extensors 1.6 times more than the maximal available strength, knee extensors more than 1.2 times more than the maximal available strength and the ankle plantar flexors 4.6 times more than the maximal available strength. It may appear that the ankle plantar flexors have compensated the most on the contra-lateral limb in the STS transfer. However, it needs to be noted that the strength of the ankle plantar flexors may be underestimated by the position of testing this group of muscles in the present study. This might be the case because generally the ankle plantar flexors are capable of supporting the total body weight while standing on toes (the average weight of the TTA group patients was 95.5 kg, whereas the mean plantar flexor strength was 13.8 kg force and this discrepancy can explain).

Overall, the automatic compensatory adaptations were reflected in the larger contra-lateral lower extremity joint moments (53.9% hip, 56.5% knee & 53.3% ankle) compared to the contra-lateral limb and increased weight-bearing on the contra-lateral foot throughout the movement.

Although the impact of major unilateral amputation such as TTA was evident in the compensatory strategy adopted by these patients for a successful STS transfer, healed unilateral PFA did not affect the (symmetrical) performance of the movement. It is therefore reasonable to presume that the plantar flexor moment produced by the amputated foot despite its decreased length (e.g.trans-metatarsal) or the altered shape (e.g.ray amputation) was adequate for a symmetrical and successful STS transfer. The decreased sensory input caused by the reduced surface area of the foot following PFA did not seem to affect the distribution of the weight-bearing during the STS task either.

Although unilateral PFA did not affect the performance of the STS task, it was interesting to note that the DFU group was another group to be affected in addition to the TTA group. These patients seemed to rely more on the contra-lateral ankle (26% greater affected ankle moment compared to the DMPN group) in an apparent attempt to safeguard the ulcerated foot (irrespective of the location of the plantar ulceration). However, the compensatory strategy did not show itself in the knee or the hip moments.

Further specific comparison of the two groups with unilateral foot disorder i.e. the DFU and the PFA group did not reveal any differences in the performance of STS transfer. However comparison between the group with minor amputation i.e. PFA and the group with major amputation i.e. TTA demonstrated variation in the STS task performance. The TTA group showed significantly less knee and hip moments on the affected limb and significantly high ankle and hip moments on the contra-lateral limb compared to the PFA group. The average values of the hip, knee and ankle moments on the affected and the contra-lateral limb of the PFA group appeared to be of similar magnitude. These findings confirmed the speculation that minor amputations i.e. PFA did not affect the performance of the STS transfer. Major amputations i.e. TTA caused asymmetry in the movement demonstrating decreased knee and hip joint moments on the amputated limb with compensatory increase in the ankle and hip moments on the contra-lateral limb.

To summarise the PFA group performed on a par with the DMPN group. However unilateral healed major amputation i.e. TTA and active unilateral DFU affected the kinetics of the STS transfer resulting in an asymmetrical weight-bearing in both groups and increased net joint moments on the contra-lateral limb of the TTA group. Within the two groups affected, the TTA group was affected more than the DFU group.

These findings may tempt the rehabilitation therapists to adopt measures to correct the asymmetry noted in the kinetics (net joint moments and weight-bearing) of the STS transfer in these patient groups. However, it is important to argue whether attempts to accomplish a symmetrical STS transfer would benefit these patient groups. In the DFU group, the compensatory strategy potentially safeguards the ulcerated foot with the intention of allowing the ulcer to heal. The adaptations noted in the TTA group appear to contribute to the stability of the movement to ensure successful completion of the movement. Although it appears that, the argument tilts in favour of restoring asymmetry, it is deemed essential to consider measures to reduce the increased net joint moments on the contra-lateral limb in the interest of protecting the aging joints from excessive joint reaction forces caused by the compensatory strategy.

It is already established that older subjects use a greater percentage of maximum muscular activity than the younger subjects to rise form the standard chair (Wheeler et al. 1985) probably because of the strength differences between the two age groups (Larsson 1978). Additionally the net joint moments of the lower extremity cannot be underestimated in magnitude compared to the other common activities required for ambulant mobility. The lower limb moments are of approximately the same level when going up and down the stairs as during rising (Andriacchi et al. 1980) or even greater at the hip during chair-rising than during stair-climbing or level walking (Rodosky, Andriacchi & Andersson 1989). Large joint moments require greater muscle force causing an increase in the joint reaction forces (JRF) (Andriacchi et al. 1980). Considering the underlying degenerative changes occurring in the aging joints any factor causing an increase in the JRF among the elderly population should be treated with concern. Moreover, the multi-system nature of DM (Holmboe 2002) also poses a challenge to the physical fitness of an individual. It may be reasonable to expect that the increased muscle activity required for a movement as common and essential as STS may contribute to a rise in the daily energy expenditure (although very little). Ultimately, increased energy expenditure might limit their performance of ADL even if the task takes an average of 1.5 to 2 s for completion.

5.3B: Quiet standing:

Balance is not recognised as an isolated quality but underlines our capacity to undertake a wide range of activities that constitute normal daily life (Huxham 2001). It forms the foundation for all voluntary motor skills (Massion & Woollacott 1996).

Balance requires the central integration of afferent information arising from three peripheral sensory systems: the vestibular organs, visual apparatus and the somatosensory receptors (Nasher 1976, Brandt 1988). Diabetic polyneuropathy is associated with bilateral sensory loss in the feet (Simmons, Richardson & Pozos 1997). Loss of movement perception at the ankle joint is found in addition to the cutaneous sensory loss secondary to diabetic neuropathy (Simoneau et al. 1996). Diabetic neuropathy is also known to cause impairment in muscle spindle function, which could either indicate a loss of afferent or gamma efferent nerves to muscle spindles in the lower leg or the damage of the spindle receptors due to diabetes mellitus (van Deursen et al. 1998). Although the exact mechanism underlying the impairment of muscle spindle function in diabetic neuropathy is not clear, the role of muscle spindles of the lower leg in postural control by providing information about the movement around the ankle joint is already known (Pyykko et al. 1989). These changes occurring in the neuro-muscular system indicate that the loss of muscle spindle function in the lower leg, loss of movement perception at the ankle and loss of plantar cutaneous sensation- all 3 factors can contribute to the impaired balance in diabetic neuropathic patients.

Therefore, it is not surprising that diabetic sensory neuropathy produces significant instability during normal stance (Cavanagh et al. 1992). Several studies have confirmed the impaired balance in standing posture resulting in patients with diabetic peripheral neuropathy (Cavanagh, Simoneau & Ulbrecht 1993, Uccioli et al. 1995, Giacomini et al. 1996, Katoulis et al. 1997). It is also known that diabetic neuropathic patients feel less safe while standing (Cavanagh et al. 1992).

The results of the present study demonstrate further deterioration of standing balance with diabetic foot ulceration, partial foot amputation and trans-tibial amputation in the presence of DMPN. Significant linear contrast between the four groups indicated a steady decline in stability with consequent stages of foot complications.

The findings reported by Ekdahl et al. demonstrate a low mean value of COP excursion (0.55m) in healthy non-diabetic subjects (Ekdahl, Jarnlo & Andersson 1989) compared to the DMPN group (0.78m) of the present study. A descriptive comparison of the results between the non-diabetic healthy controls and the four diabetic groups of the present study demonstrate a steady increase in the excursion of COP from non-diabetic healthy subjects (0.55m) to patients with DMPN (0.78m) to DFU (1.12m) to PFA (1.16m) to TTA (1.08m).

It is evident that all 4 groups already present with compromised sensory and proprioceptive input in the feet due to DMPN. Bilateral cutaneous sensory deficit in the feet and abnormal proprioceptive input from the lower extremities are both known to contribute to the postural instability of the patients with DMPN (Katoulis et al. 1997, Simmons 1997). Superimposition of mechanical disruption of plantar tissues in the form of unilateral plantar ulceration contributes to further progression of instability. Although it may be argued that diabetic patients with insensate sensory neuropathy (none of the patients in this study sample presented with painful neuropathy) should not be affected by the presence of plantar ulceration during standing, 30.36 % greater excursion of COP in the DFU group clearly indicates the substantial negative impact of ulceration on standing balance. Previous studies have already confirmed the increased postural instability in patients with prior ulceration compared to those without history of foot ulcers (Katoulis et al. 1997). These observations suggest that the further impairment in sensory feedback due to plantar ulceration is more likely to be the cause for decline in standing balance than merely the discomfort due to ulceration.

Researchers have already acknowledged the contribution of the mechanoreceptors located in the skin to the somato-sensory information necessary to maintain balance in standing (Kennedy & Inglis 2002). Input from the sensory end-organs of the tendons and the muscle is also necessary for maintenance of balance (Wyke 1972). Complete loss of sensory input from the cutaneous plantar tissue (minimum surface area= $0.1mm^2$, maximum surface area= $11\ mm^2$) in all the patients and loss of feedback from the sensory end-organs of the tendons and the muscles in few patients (patients with bone-deep ulceration, n=2) can explain the decreased stability in this group. Moreover, the non-ulcerated plantar tissues in the remaining surface area are already compromised in sensory function. Additionally, the presence of bulky dressings could further dampen the sensory feedback from the non-ulcerated plantar tissue by occupying an excess of the plantar surface area surrounding the ulcer. Currently there is no direct evidence to support this contention. However, there is a report, which demonstrates that body sway increased with age when the subjects with peripheral neuropathy stood on a rubber foam but not on the firm platform (Bergin et al. 1995). Therefore, the practice of bulky dressings or padded hosiery in the healing of the ulcer with the intention of providing protection needs to be researched to investigate its impact on the balance of diabetic patients with compromised sensory feedback.

Patients with consequent stage of foot complication i.e. partial foot amputation demonstrated a further decline in standing balance. Normally during quiet, level standing the centre of gravity projects approximately 5cm anterior to the axis of the ankle joint. The length of the foot is known to resist the tendency to fall from the continous antero-postero oscillations during quiet standing (Saltzman & Nawoczenski 1995). Effectively the decreased base of support resulting from either a short foot (as a result of trans-metatarsal amputation) or a deformed foot (ray amputations, toe amputations) may explain the increase in instability of this group. Moreover, it is known that most of the support and balance in standing comes from passive structures e.g. the bony architecture and multiple different axes of joint motions (Saltzman & Nawoczenski 1995). Therefore, alterations in the architecture of the residual foot can explain the detrimental effect on the residual foot to support the body during standing. Additionally, the reduction in the total plantar surface area also ultimately decreases the residual sensory feedback from the amputated foot.

It is also speculated that the choice of orthosis could influence balance in the standing position. However, the probable effect of orthoses on standing balance in the present study can be ruled out since all the patients were examined in standard footwear with a shoe-filler. Further investigation in this area is necessary to explore the role of appropriate footwear in the facilitation of postural stability in patients with PFA.

With the same premise that impaired or partial loss of sensory feedback from the affected foot causes deterioration in standing balance, the TTA group would be expected to demonstrate the most severe affection of standing balance. However, it was interesting to note that the mean values of COP excursion of the DFU and PFA groups were higher compared to the TTA group, although the mean value of the DMPN group was low compared to the TTA group. TTA cannot be treated as merely the absence of a part of the extremity but is also a peripheral sensory disorder. Complete loss of sensory feedback from the amputated limb and impaired sensory feedback from the contra-lateral limb can be expected to contribute to substantial postural instability in these patients.

One would have imagined that the impairment in standing balance would be severe in patients with TTA compared to patients with PFA because of the complete loss of the plantar cutaneous sensory input, ankle proprioception and muscle spindle function of the lower leg on the amputated side. However statistical comparison of COP excursion between minor amputations i.e. PFA vs major amputation i.e. TTA did not reveal a significant difference.

Researchers in the past have confirmed that trans-tibial amputee patients (male) with DM sway more than healthy subjects (Isakov et al. 1992). However it is promising to learn that rehabilitation training is known to result in improvement of balance control (particularly for the dual-task condition), indicating an attempt towards restoration of automaticity of postural control as an essential characteristic of the central reorganisation process in persons with LEA (Geurts et al. 1991). Unfortunately, rehabilitation following foot amputations is still not clearly defined. Current clinical practice is reflective of the lack of efforts in the balance training of patients with PFA. Therefore, the apparent better stability in the TTA group (based on average values of COP excursion between the 2 groups) can be attributed to the defined rehabilitation care for patients with trans-tibial amputations as against patients with PFA.

All the patients belonging to the TTA group were rehabilitated at the Artificial Limb and Appliance Centre (ALAC) post-amputation and had completed a minimum of 6 months following their discharge from the ALAC. Balance training was an integral part of the rehabilitation programme designed for these patients. Whereas none of the patients belonging to the PFA group had received any form of training after the foot amputation. Therefore, it is reasonable to speculate that the actual difference between the stability of the PFA and the TTA group was masked by the training of the TTA group, which ultimately resulted in statistical non-significance of the results.

Currently the management of PFA appears to end by defining the success of the procedure as retaining the foot and providing a prosthesis-free 'normal gait' (Hosch, Quiroga, Bosma, Peters, Armstrong & Lavery 1997). However, the findings from the present study highlight that it is not sufficient to salvage the foot for ambulation alone but it is necessary to provide a rehabilitation plan for these patients to improve their balance.

It was also interesting to investigate whether the DFU group (which presented with mechanical disruption of plantar surface area) and the PFA group (which presented with anatomical loss of a particular area of the foot) varied in their stability. However, comparison of COP excursion between the 2 groups did not reveal significant difference, indicating that probably plantar tissue injury and partial loss of the foot did not have a different impact on the standing balance.

Considering the severe loss of sensations in the DFU, PFA and TTA groups, the likely influence of neuropathy score on the excursion of the COP was examined to investigate whether the decline in balance was due to the severity of neuropathy or it was an effect of the progression of foot complications.

There was a significant difference in the standing balance between subjects (from all 4 groups i.e. DMPN, DFU, PFA & TTA) with different neuropathy score (0,1,2,3). Comparison between the neuropathy score and the COP excursion demonstrated that patients with complete sensory loss (0) were more unstable than patients with diminished sensory loss. However, among patients with diminished sensory loss (1,2,3) there was no trend between the severity of neuropathy and the excursion of COP. These findings indicate that even if the patients have some (diminished) sensory feedback available from their feet they are able to maintain better postural stability compared to those with complete sensory loss. Therefore, the deterioration in balance in the three groups with further foot complications can partly be attributed to the greater number of patients with complete sensory loss in those groups compared to the DMPN group. Although it is not possible to comment on the precise association between the severity of neuropathy and the deterioration in balance based on our results, the findings suggest that patients with complete sensory loss have severe instability compared to patients with diminished sensory loss. These results concur with the findings reported by Boucher et al 1995, which demonstrated that patients with moderate to severe neuropathy (n=6) presented with greater postural instability compared to those with mild neuropathy (n=6).

The authors noted that even with vision, the postural stability of neuropathic patients is impaired and may put them at higher risk of falling when performing more challenging daily tasks (Boucher et al. 1995). The significant correlation between the neuropathy score and the COP excursion in the DMPN group alone and the finding reported by Boucher et al. (1995) confirms the fact that the neuropathy score is associated with postural stability. However, the lack of association between the neuropathy scores and standing balance in patients with DFU, PFA and TTA suggests that the further impact of consequent stages of foot complications superseded the influence of neuropathy score on balance. Based on the significant decline in balance across 4 diabetic neuropathic groups and the correlation between the neuropathy score and standing balance in the DMPN group alone, it may be reasonable to presume that the impact of progression of foot complications due to DMPN on the postural stability is far more evident than the severity of neuropathy.

The consequences of instability have already been evaluated in this patient population. Patients with DMPN demonstrate significant balance loss associated with cutaneous deficit in the foot placing them at an increased risk of falling (Yamamoto, Kinoshita, Momoki, Arai, Okamura, Hirao & Sekihara 2001). Similarly, patients with prior DFU are already known to be at a risk of falls, a small percentage of falls resulting in fractures (12.4 fractures/1,000 persons-years in men, 40.2 fractures /1,000 persons-years in women) (Wallace et al. 2002). However, there is no evidence to describe the risk of falls in diabetic patients with current foot ulceration or PFA. It would be interesting to compare the incidence of falls in these four patient groups. Concurrently the findings from the present study warrant an urgent need for introducing balance retraining in patients with DMPN, plantar ulceration and partial foot amputations.

To summarize the findings of the present study demonstrate that there is a significant decline in standing balance with progression of foot complications secondary to diabetic neuropathy. However, it is interesting to note that the PFA group demonstrated a greater value of the excursion of the COP compared to the TTA group indicating greater instability although the difference was not statistically significant. Further investigation with a larger sample size is necessary to confirm this observation. In the meanwhile, these preliminary results can be used to inform clinical practice about the urgent need for rehabilitation of the patients following PFA including balance training as much as training of the patients following TTA.

5.3C: Gait:

Walking was the next task of mobility to be studied. The findings from the present study are in agreement with the results from the previous studies analysing gait in patients with DMPN, PFA and TTA. Additionally these findings describe the gait pattern of patients with current plantar ulceration and allow comparison of the gait pattern between the 4 groups of patients at subsequent stages of diabetic foot complications.

The results demonstrated a significant decline in the gait velocity, cadence and stride length from the DMPN to DFU to PFA to TTA group. However, specific comparisons between the DFU vs. PFA groups and PFA vs. TTA groups did not demonstrate differences in gait velocity, cadence and stride length. The statistical non-significance can be attributed to the inadequate sample size since the power of the test was estimated for the primary comparison between the 4 groups.

Patients with DMPN are reported to walk with slow speed, decreased cadence and short strides compared to their non-diabetic age-matched counterparts (Mueller et al. 1994, Courtemanche et al. 1996, Dingwell et al. 2000, Menz et al. 2004). Descriptive comparison of the results of gait velocity from the diabetic neuropathic patients with the healthy non-diabetic subjects demonstrates that there is a decline in the gait velocity from the healthy subjects to the diabetic neuropathic patient groups with consequent foot complications (refer Figure 4.12). Despite the difference in the methodology, the values were comparable to previous reports (Mueller et al. 1994, Courtemanche et al. 1996). Courtemanche (1996) reported a mean gait velocity of 1.32m/s and mean cadence of 103 steps/min. Mueller (1994) reported a mean gait velocity of 1.06 m/s, mean cadence of 106 steps/min and mean stride length of 1.20m. Descriptive comparison of the diabetic neuropathic groups with the healthy subjects presented in Figure 4.12 demonstrated a consistent decline in gait velocity from healthy non-diabetic subjects (1.32 m/s) to DMPN patients (1.13 m/s) to DFU patients (0.91 m/s) to PFA patients (0.87 m/s) to patients with TTA (0.74 m/s).

Owing to proprioceptive deficit resulting from DMPN, these patients walk with a slower and more conservative gait pattern than non-diabetic patients (Courtemanche et al. 1996). Reduction in walking speed is a compensatory strategy used by the neuropathic patients to maintain the dynamic stability of the upper body during level walking (Dingwell, Cusumano, Sternad & Cavanagh 2000). However, despite adopting a more conservative gait pattern these patients have an impaired ability to stabilize their body when walking on irregular surfaces (Menz, Lord, St George & Fitzpatrick 2004). The increased attention demands in gait of diabetic neuropathic subjects indicate that the diminished sensory information makes gait more cognitively dependent compared to non-diabetic subjects. It is speculated that a deterioration of peripheral sensory systems could potentiate gait and balance problems because of increasing attention demands for the postural tasks (Courtemanche et al. 1996). It has been shown that diabetic neuropathic patients also feel less safe in standing and walking (Cavanagh et al. 1992). These challenges faced during walking could explain the increased risk of falls in diabetic neuropathic patients (Yamamoto, Kinoshita, Momoki, Arai, Okamura, Hirao & Sekihara 2001).

Further to the somato-sensory deficit resulting from DMPN, presence of plantar ulceration appears to make the conservative features of the gait pattern more pronounced. The reasons for such a pronounced conservative gait pattern in these patients could be several. It could be argued that they walk slower because of the increased instability resulting from plantar ulceration or they feel less safe during walking or it is a conscious attempt to safeguard the ulcer or the discomfort caused by the ulcer on the plantar surface limits their ability to walk. The results from the COP excursion from the present study underpin the argument that postural instability of diabetic patients with peripheral neuropathy increases further with plantar ulceration in standing. A pronounced conservative gait pattern may occur as a result of a compensatory strategy adopted by these patients to maintain stability during walking. Speculations regarding a feeling of less safety during walking or patient's conscious discretion to attempt to walk slower to safeguard the ulcer need further investigation. However, it was confirmed that patients were not instructed by the members of the foot care team to walk slower. Patients were asked to describe the instructions given to them about their walking activity and none of the patients reported that they were instructed to walk slower. Although the understanding of the precise mechanism underlying such a gait pattern in diabetic neuropathic patients with plantar ulceration warrants further research, it is reasonable to expect that it would be a combination of these factors.

Patients with PFA demonstrated a further decrease in gait velocity and stride length although the mean value of the cadence was marginally higher compared to patients with

DFU. However, on comparing the PFA group with the DFU group none of the three parameters revealed a significant difference. In addition, it was interesting to note that the comparison between the PFA and TTA group did not reveal a significant difference. Based on these observations, it can be inferred that either the impact of minor or major amputations and plantar ulceration or partial foot amputation on the spatial and temporal parameters of gait did not vary or this was an effect of inadequate power of the test in the present study. In case of the latter possibility, further studies with larger sample size should be performed to explore the differences between these groups.

On revisiting the results of the PFA group, it is necessary to mention that the gait findings of the PFA group from the present study concur with the results reported previously. Mueller et al. (1998) reported a gait velocity of 0.86 m/s (0.87 m/s from the present study) and a step length of 0.43 m (stride length=1.07m) in diabetic subjects with TMA (Mueller, Salsich & Bastian 1998). It is speculated that the biomechanical alterations produced in the ankle-foot complex along with the increased postural instability because of PFA may contribute to the slow gait. Although the PFA group was not directly compared with the DMPN group the decline in the average COP excursion from the DMPN to PFA group may hint that the more severe postural instability can contribute to the slower gait.

Secondly, the ankle plantar flexors are known to generate 70% of the power during the push-off of the gait cycle. Shorter lever arm of the foot can contribute to the inability of the ankle on the amputated limb to generate adequate power at push-off (Mueller, Salsich & Bastian 1998) effectively slowing down the gait.

Patients with TTA demonstrated a further deterioration in gait velocity, cadence and stride length. There is hardly any evidence with which to compare the results of the present study in the diabetic population. Most studies in the past have classified diabetic amputee patients as vascular amputee patients with the objective of comparing their gait pattern with traumatic amputee patients. Therefore, the closest available comparison was with the results reported by Winter et al. (1988). The authors did not describe the causes for amputation and neither the average age of the participants mentioned. They reported an average gait velocity of 0.97 m/s and an average cadence of 92 steps/min (Winter & Sienko 1988). Complete loss of the ankle-foot complex necessary to generate the power at the ankle can explain the slower gait pattern in patients with TTA in the present study. Moreover, the weakness of the muscles around the knee of the amputated limb and the ankle on the contra-lateral side can also contribute to the slower gait pattern of these patients.

Further to describing the spatial and temporal parameters of the gait cycle, lower extremity joint moments were evaluated to understand the kinetics of the gait cycle in these patient groups. The hip, knee and the ankle joint moments were studied. Gait velocity was used as a co-variate in the analyses of lower extremity joint moments since it is known to influence these gait parameters (Andriacchi, Ogle & Galante 1977). The peak ankle plantar flexor moments and the knee moments on the affected limb were significantly different between the 4 groups. The average affected ankle moments showed a decline from DMPN to DFU to PFA groups with a high mean value of the TTA group compared to the mean of the PFA group. However, the linear polynomial contrast across the four groups was non-significant. The average knee moments on the affected limb showed a gradual rise except for the TTA group, which demonstrated the lowest mean value. Even the knee joint moments on the affected limb did not demonstrate a significant linear contrast across the four groups. The hip moments on both limbs did not reveal significant difference between the 4 groups.

Specific comparison between the DFU and PFA groups revealed a significant difference in the net ankle joint moments on the affected limb. The PFA and the TTA groups significantly varied in the net ankle and knee joint moments on the affected limb.

Previous researchers have reported that the DMPN group walked apparently with a hip strategy i.e. they appeared to pull their leg forward using the hip flexor muscles rather than pushing their leg forward using the plantar flexor muscles i.e. ankle strategy. The authors attributed the changes in gait to decreased muscle strength and mobility at the ankle in patients with DM (Mueller et al.1994). However, it is difficult to comment on the specific gait strategy adopted by patients in the present study since the ankle and hip moments were recorded at different phases of the gait cycle.

However, the steady decline in the group means of the net ankle plantar flexor moment during push-off from the DMPN to DFU to PFA group (although non-significant) clearly suggests the inadequate push-off during walking. The DFU group demonstrated a decrease of 13.1 % compared to DMPN group, whereas the PFA group demonstrated a decrease of 35.2 % in the average peak ankle plantar flexor moment compared to DMPN group.
Slower gait velocity along with the tendency to protect the ulcerated foot can explain the inadequate push-off in patients with DFU.

In the case of patients with PFA, the short lever arm of the foot is known to contribute to the inability of the ankle on the amputated limb to generate adequate power at push-off (Mueller, Salsich & Bastian 1998). The same study reported a 25% reduction in ankle push-off power of the diabetic PFA patients compared to the non-diabetic age-matched controls (Mueller, Salsich & Bastian 1998) but the authors could not confirm whether the effect was due to the PFA or the DMPN. However, the findings of the present study rule out the contribution of somato-sensory deficit alone in the reduction of net ankle joint moments because of the presence of DMPN in all the four groups. All the groups included established cases of DMPN although there were differences in the level of severity of the neuropathy. Moreover, exclusive reduction in the net ankle plantar flexor moment only on the affected limb across the groups (DFU: affected vs contra-lateral=111.4 vs 131.2 N.m & PFA: affected vs contra-lateral=83.0 vs 118.5 N.m) strengthens the argument that, it is more likely to be an effect of the ulceration and partial foot amputation than peripheral neuropathy, which demonstrated a bilateral presentation. The DMPN group demonstrated average ankle plantar flexor moments of similar magnitude on both the sides (affected vs contra-lateral=128.0 vs 124.8 N.m).

The significant difference in knee joint moment between the four groups could be attributed to the notable low average knee moments on the affected limb of the TTA group during the loading phase of the gait cycle. Such an observation can be explained by the substantially low strength of the knee extensors on the affected limb of this group (29% less than DMPN) and the reduced loading of the prosthetic limb. Moreover, 29% slower gait velocity of the TTA group can also contribute to the low average knee moments. The reduced loading on the knee can be attributed to the less ability of the prosthetic limb to support the body weight (Suzuki 1972). Furthermore previous studies have documented that the patients with TTA demonstrate a negligible moment of force and reduced mechanical power at the knee during gait analysis (Czerniecki, Gitter & Munro 1991, Gitter, Czerniecki & Degroot 1991).

Lack of studies evaluating gait in diabetic neuropathic amputees with similar methodology limited the comparison of the findings from the present study with previous reports. However Winter et al.(1988) confirmed that the patients with below-knee amputations had hyperactive hip extensor during early and mid stance to partially compensate for the lack of energy generation by the plantar flexors at push-off.

Both the specific group comparisons i.e. DFU vs. PFA and PFA vs. TTA demonstrated significantly lower ankle joint moments of the PFA group when compared to the DFU and the TTA group respectively. Low peak ankle plantar flexor moments in the PFA group compared to the DFU group suggest that the ankle-foot complex is more inefficient in producing a push-off due to a short lever arm (from a shortened foot) than the foot which is intact but has an ulcer on the plantar surface. The TTA group would have been expected to demonstrate the least ankle moments because of the presence of the prosthetic ankle. However, it was interesting to note that the prosthetic ankle moments in the TTA group were significantly higher compared to the PFA group. Such an observation could result from the participation of the prosthetic ankle-foot complex in the gait produced by the stretch of the elastic materials generating a moment, which is trained to suit the requirement of the gait. However, the loading of the knee on the amputated limb (TTA group) remained significantly low compared to the PFA group, which has an intact distal lever arm provided by the leg. It is speculated that although the extensor apparatus of the knee (which helps to contribute to the loading of the knee during the stance phase of the gait cycle) is retained in case of a trans-tibial amputation, the lack of the ankle plantarflexor apparatus to control the forward rotation of the leg over the foot might explain the decreased loading on the knee joint of the amputated limb during the stance phase of the gait cycle.

In terms of symmetry of weight-distribution during walking, it was observed that there was a significant increase in the GRF on the contra-lateral limb from the DMPN to TTA group. Ground reaction force of almost 0.7 times the body weight on the contra-lateral limb of the DFU group patients and PFA group patients and 0.8 times body weight on the contra-lateral limb of the TTA group patients was a clear indication of marked asymmetry in weight-bearing during walking, despite a significant decline in gait velocity across the 4 groups ($p<0.001$). Even if the element of targeting the force plate during walking was considered in the interpretation of these findings, the proportionately high magnitude of the weight-bearing force with respect to the body weight confirms the aymmetric loading of the limbs during walking. Because it is already established that the effects of targeting (in terms of magnitude of peak ground reaction forces) are present within the first half of the gait cycle only. During the second half or propulsive phase the pattern of push off force is unaltered. Moreover, the authors confirm that the changes to the GRF were quite small and therefore excessive concern about targeting in measurement of biomechanical variables may not be warranted (Sanderson, Franks & Elliott 1993).

On revisiting the asymmetric pattern of limb loading, it is observed that such a gait pattern is similar to the pattern noticed during an antalgic gait. McCrory et al. (2001) has reported less magnitude of peak ground reaction force on the affected limb of the subjects with hip athroplasty compared to their unaffected limb and to the control group (normal healthy subjects) (McCrory, White & Lifeso 2001). The asymmetric loading of the lower limbs observed in the present study drives the discussion to the question whether patients with DFU, PFA and TTA should be trained to walk with equal weight-bearing. Although therapists may be tempted to correct the asymmetry, they may be cautious in case of patients with DFU because such a gait pattern is actually contributing to offload the affected foot on one hand. Whereas on the other hand, it needs to be recognised that although the gait pattern may appear to benefit the patients during the phase of wound healing, the additional stress on the contra-lateral limb for a prolonged period (average healing period=13.4 months) may eventually lead to osteoarthritic changes in the contra-lateral limb as demonstrated earlier in other musculo-skeletal conditions (Dekel & Weissman 1978, Radin et al. 1978, Arsever & Bole 1986, Suter et al. 1998). Similarly, patients with PFA and TTA may predispose the joints of the contra-lateral limb to degenerative changes due to increased loading. Therefore, it may be advisable to strengthen the lower limb muscles adequately and walk with adequate foot protection and measures to ensure stability e.g. walking stick during walking rather than attempting to correct the asymmetry.

However, the substantial increase in the weight-bearing force on the contra-lateral limb in the present study did not correspond with the net joint moments on the contra-lateral limb during walking. There was a slight increase in the average ankle joint moments of the DFU, PFA, TTA groups and hip joint moments of the TTA group on the contra-lateral limb compared to the affected limb. However, the percentage of rise in the lower limb joint moments did not correspond with the notable increase in weight-bearing on the contra-lateral limb of all these 3 groups of patients with further unilateral foot complications.

To summarize, the present findings demonstrate a decline in gait velocity, cadence and stride length with progression of diabetic foot complications. The gait pattern turns more conservative in diabetic neuropathic patients with plantar ulceration; partial foot amputation and major LEA such as TTA compared to patients with DMPN alone. In addition to the mechanical impairment caused by further foot complications secondary to DMPN, the muscle weakness also contributes to the slow pattern of gait demonstrated by the TTA group which is affected the most.

The results from the analysis of the net joint moments demonstrate that there was a decline in the ankle plantar flexor moments across the 4 groups which can be partly explained by the significant decline in the gait velocity. However, specific group comparisons (DFU vs PFA, PFA vs TTA) demonstrated that, although there was a decline in the ankle plantar flexor moments across the 4 groups, the effect of the short and biomechanically inefficient lever arm of the foot following PFA was significant in reducing the peak ankle plantar flexor moment compared to the effect of plantar ulceration or the artificial ankle-foot prosthetic complex. Additionally, it was also noted that TTA group walked with less average knee moment on the affected limb compared to the PFA group. This could be the case due to the lack of the ankle plantarflexor apparatus of the TTA group to control the forward rotation of the leg over the foot during the stance phase of the gait cycle, other than the fact that the TTA group appeared to walk slower compared to the PFA group (based on the average values and the significant contrast).

5.3D: Self-reported measure of mobility: Rivermead Mobility Index (RMI):

Following a battery of performance based tests evaluating the various tasks of mobility; it was interesting to note the results from the self-reported measure of mobility. RMI score demonstrated a significant difference between the four groups. The DMPN group scored the maximum whereas the TTA group scored the lowest. Both the DFU and PFA groups reported exactly the same score which was 13.3% less compared to the DMPN group.

Specific group comparisons i.e. DFU vs. PFA and PFA vs. TTA groups did not reveal significant differences.

The findings from the present study illustrate a probable ceiling effect of the RMI within the DMPN group as 69.6% (16/23) of the patients belonging to the DMPN group scored full score i.e. 15/15. Such an observation indicates that the DMPN group actually could have performed better in terms of mobility than measured by the RMI.

Lack of previous studies using RMI to grade the level of mobility in diabetic neuropathic patients made it difficult to compare the results of the present study. Regardless of its application in diabetic population, there is no standardised data to grade the level of mobility based on the RMI score in various age groups. Lack of such information, probably can be explained by the hierarchical ordering of items and the presence of inter-item dependency between the items 3 and 15 making it difficult for cross-diagnostic validity (Ryall et al. 2003). However, there have been attempts to measure mobility of the patients with lower limb amputations using RMI around the same time as this report was published (Franchignoni, Brunelli, Orlandini, Ferriero & Traballesi 2003, Ryall, Eyres, Neumann, Bhakta & Tennant 2003). Ryall et al. (2003) documented an overall median score of 12 in their study. Despite the wide range of age (13-88 yrs) and cause of amputations (trauma, PVD, infection, congenital, cancer and DM) and the mixture of the unilateral and bilateral amputees in their study, the overall median score was very close to the median score of the TTA group of the present study (RMI=11.5). Age, cause of amputation and level of amputation (unilateral/bilateral) can be identified as potential factors in the determination of mobility in patients with LEA (Johnson, Kondziela & Gottschalk 1995, Treweek &

Condie 1998, Turney et al. 2001, Kauzlaric, Sekelj-Kauzlaric & Jelic 2002, Davies & Datta 2003, Fisher, Hanspal & Marks 2003).

The similar score between the two studies hints towards the probability that RMI lacks the ability to discriminate the influence of age, cause of amputation and level of amputation. Moreover, even the present study did not demonstrate difference in mobility of the patients with minor amputations (PFA) and major amputations (TTA) on the RMI whereas the two groups varied significantly based on the other performance based measures such as- sit-to-stand performance, cadence and average daily strides. Such an observation casts a doubt on the use of RMI in investigating the influence of level of LEA on the level of mobility of amputee patients, which could be due to the lack of the sensitivity of the tool.

Further more when Franchignoni et al. applied RMI in lower limb amputees they reported that it is an ordinal measure with adequate levels of a series of psychometric properties, which seems more useful for epidemiological studies than for everyday clinical application in single patients (Franchignoni, Brunelli, Orlandini, Ferriero & Traballesi 2003). Lenon & Hastings (1996) emphasised the limitation of the binary response of the RMI items. As it was scored on a 'yes' (1) or 'no' (0) basis, it failed to be sensitive to small changes that occur during the patients recovery (Lennon & Hastings 1996).

However, the ability of the RMI score to provide useful information from epidemiological studies indicates that the findings of the present study can provide the baseline information of self-reported measure of mobility in diabetic neuropathic patients. Moreover, the trend in the RMI score across the 4 groups was similar to the trend observed in other performance based measures of mobility, such as gait velocity, cadence and average daily strides. The highest score of the DMPN group, lowest score of the TTA group and comparable scores of the DFU and PFA groups are consistent with the overall findings from the performance-based measures of mobility. It was interesting to note that even the patient's perception of the limitations caused by the presence of a foot ulcer and absence of a part of the foot on their overall body mobility was similar to the limitations demonstrated by the performance-based measures. Although it was not intended to investigate the association between RMI (self-reported measure) and the performance-based measures of mobility statistically within the present study, the consistence in the pattern of findings between the two types of measures used to evaluate mobility supports the validity of the tool in this patient population. It also helps to make a choice regarding the outcome measure to be used in clinical practice. In case of sufficient agreement (which is purely based on descriptive comparison) between the performance-based and self-reported measures, not all of them need to be measured to arrive at a conclusion regarding the functional outcome. However further research would be necessary to examine the validity of the tool in the specific patient groups.

5.3E: Summary of the findings from the domain of mobility:

To summarise the findings from various mobility tasks (measured with self-reported and performance-based measures), the present study demonstrated that there is a decline in the overall mobility of the patient groups from DMPN to DFU to PFA to TTA in terms of

i) balance in standing position, ii) characteristics of gait pattern and iii) the impact of essential mobility tasks such as rising from a chair and walking on the lower limb joint moments. However, it needs to be noted that the patients attempted to compensate with the contra-lateral limb for the inefficiency of the affected limb wherever possible such as the STS task.

While performing the STS task, the increasing level of difficulty encountered with the progression of foot complications was reflected in the decreasing net joint moments of the affected ankle, knee and hip despite rising from a reasonably high chair. However, the patients managed to execute the task by demonstrating a compensatory increase in net joint moments on the contra-lateral ankle and hip.

A steady decline in standing balance with consequent stages of foot complications demands greater emphasis and implementation of rehabilitation training to improve balance in all these patient groups with specific emphasis on patients with PFA and DFU, which appear to be more unstable than the TTA group. Appropriate measures need to be defined and evaluated for these patient groups.

The gait cycle demonstrated an increasingly conservative pattern with progression of foot complications, which can be partly attributed to the weakness of the muscles around the knee and the ankle. Although the walking pattern was conservative, it needs to be highlighted that such a pattern can help to restore the postural stability of the diabetic neuropathic patients and also safeguard the neuropathic foot from a potentially increased risk of injury caused by faster gait speed. In addition to slowing down gait the consequent foot complications also showed their influence on the ankle joint moments which decreased significantly on the affected limb. It was interesting to note that although there was a decline in the ankle plantar flexor moments across the 4 groups, the effect of the short and biomechanically inefficient lever arm of the foot following PFA was significant in demonstrating an inefficient push-off compared to the effect of plantar ulceration or the artificial ankle-foot prosthetic complex.

Even the findings from the self-reported measure of mobility, i.e. RMI, agreed with those from the performance-based measures demonstrating a significant difference in the mobility of the 4 groups, with the DMPN group performing the best whereas the TTA group presenting with the lowest score.

5.4: Plantar pressure distribution:

It was crucial to study the impact of the common essential mobility tasks on plantar loading in the patient cohort, which is already at risk of plantar injury from diabetic neuropathy. The findings from the present study have indicated that the patients with unilateral manifestation of diabetic foot disease, namely unilateral DFU, PFA and TTA demonstrated a compensatory increase in the weight-bearing on the contra-lateral foot while rising from a chair. However in the light of previous evidence which demonstrates that the plantar pressures during rising and sitting in the chair are much lower compared to standing and walking (Rozema, Ulbrecht, Pammer & Cavanagh 1996) it was decided to measure the plantar pressures only during walking.

Although most of the literature has documented dynamic plantar pressure during walking, there are a few studies, which have documented plantar loading during standing in diabetic neuropathic patients. Based on the results from such past studies Gefen (2003) reported the average peak forefoot pressures under apparently normal feet of the healthy adults as 60-85 kPa. Duckworth et al. (1982) reported an average peak forefoot pressure of 140 kPa in diabetic patients (n=82). Another study reported an average peak forefoot pressure of 131 kPa in diabetic patients (n=7) (Kato et al. 1996). Based on the results of all these studies Gefen (2003) inferred that the peak pressures under the medial metatarsal heads of diabetics (average 136 kPa) are 1.5-2.3 times greater than normal during standing. These pressures rise to an average of 333 kPa in diabetic neuropathic subjects during walking as seen in the present study. A 59% raise in the peak pressures during walking probably explains why the researchers concentrate on the evaluation of pressure distribution during walking in the patients with DMPN including the present study (Veves, Vanross & Boulton 1992, Katoulis, Boulton & Raptis 1996, Armstrong & Lavery 1998).

Therefore, the findings from the plantar pressure distribution during walking in diabetic neuropathic patients with further foot complications are discussed in this study. To re-capture the methods: Maximum peak pressure (MPP), Pressure-time-integral (PTI) and Daily plantar cumulative stress (DPCS) were the three variables analysed to provide a complete picture of instantaneous peak pressure and cumulative plantar stress in these patients. Considering the influence of gait velocity on MPP (Burnfield, Few, Mohamed & Perry 2004) gait velocity was used as a covariate to compare the means of the MPP of the adjusted groups.

At this stage, it needs to be remembered that the DFU and the PFA groups were heterogeneous in terms of the site of plantar ulceration and the level of foot amputation. Therefore, the interpretation of the results of pressure distribution over specific plantar areas was limited. However, the total foot pressures can be considered as a tool to assess the risk of plantar injury and therefore the findings over the total foot area should be relied on more for the discussion. The results demonstrated a significant rise in the MPP over the total affected foot from the DMPN group to the PFA group. On the contra-lateral foot, there was a significant rise in MPP over the heel. The 1-2 MT area on the contra-lateral foot of the DFU group showed highest pressure amounting to 12.7 % higher MPP compared to the DMPN group however the difference between the groups failed to reach the statistical significance (p=0.066).

It is already established that peak plantar pressures increase with DMPN (Katoulis, Boulton, & Raptis 1996, Plank, Wilcox & Hyer 1999). Descriptive comparison of the results from the present study with the healthy subjects tested by Burnfield et al. (2004) confirm that peak plantar pressures increase with DMPN (refer normative data in the results and methods chapter). Although the DMPN group of the present study was 1.2 times heavier (which might cause higher pressures), it needs to be noted that they walked at a speed of 0.20 m/s slower (which is known to reduce MPP) compared to the healthy subjects, effectively cancelling out the two opposite effects on peak pressures and resulting in effectively higher MPP in the DMPN group. The average MPP was 66.7% higher over the med MT, 67.8% higher over the lat MT and 39.7% higher over the hallux in the DMPN group. Effectively the DMPN group of the present study demonstrated peak pressures, which were 3 times higher over the medial and lateral metatarsal regions and 1.7 times higher over the hallux, compared to the healthy adults measured by Burnfield et al. (2004). These findings re-confirm that impaired sensory feedback due to diabetic neuropathy causes the rise in peak plantar pressures and emphasise that patients with DMPN are already at risk of ulceration from neuropathy compared to the healthy adults.

The DFU group would have been expected to demonstrate higher peak pressures compared to the DMPN group. However, the difference in the average values of MPP between the DMPN & DFU group was only 2.82 kPa although the three groups (DMPN, DFU & PFA) demonstrated significant difference in MPP over the total affected foot. Such an unapparent difference between the group means of MPP may be underlined by the statistical computation of the mean MPP in the ANCOVA. The DFU group walked with significantly decreased gait velocity compared to the DMPN group. Therefore, gait velocity was used as a co-variate in the analysis of MPP since it is known that peak pressures rise with increasing gait velocity (Burnfield et al. 2000). With this conjecture, the pressures should be lower with reduced walking speed in the DFU group. However, despite walking 20% slower, the ulcerated foot presented with mean MPP comparable to the neuropathic foot. Such an observation is explained by the computation of the statistical software, which actually uses the estimated marginal means to analyse the difference in MPP after adjusting the variation in gait velocity using ANCOVA.

Regional comparison of the specific foot regions between the groups did not elucidate significant differences. As reported previously, the DFU group may be expected to demonstrate higher MPP over the forefoot where the ulcers occur commonly (Mueller 1995) compared to the DMPN group. Even a previous study documented higher MPP over the total foot (469.4 vs 359.2kPa) and specifically over the hallux (201.9 vs 120.1kPa) compared to the DFU group of the present study (Stacpoole-Shea, Shea & Lavery 1999). However, it needs to be highlighted that the patients studied Stacpoole-Shea et al. (1999) appeared to walk faster (cadence=126 steps/min). Cadence was considered as an indirect measure of speed since the previous authors have not reported the distance compared to the patients of the present study (95 steps/min) and none of those patients had ulcers over the plantar surface of the hallux, probably explaining the higher MPP over the hallux.

Moreover it needs to be emphasised that the DFU group of the present study included patients with varied locations of plantar ulceration (toe=3, 1-2 metatarso-phalangeal region=7, 3-5 metatarso-phalangeal region=6, hallux=2 and heel=5). Therefore although the majority of patients had fore-foot ulceration (n=18), the averaging effect of various sites of ulcers probably will have masked the otherwise pronounced peak pressures over the fore-foot. In order to demonstrate the possibility of the averaging effect the DFU group patients were further classified into 2 subgroups based on the site of ulceration. The higher average MPP values of the DFU subgroup with fore-foot ulceration (n=18) compared to the average MPP of the total DFU group (n=23) and the lower average MPP values of the DFU subgroup with heel ulceration (n=5) compared to the average MPP of the total DFU group (n=23) explains the likely effect of averaging of the peak pressures due to different ulcer locations (refer Table 4.36). Therefore, despite a 58% reduction of the MTP joint motion in the DFU group compared to the DMPN group, no significant rise in MPP was demonstrated over the affected fore-foot of the DFU group.

Additionally although non-significant, the peak ankle plantar flexor moments of the DFU group during push-off showed a decline of 13.1% compared to the DMPN group. Therefore, it is reasonable to assume that the patients with DFU demonstrated an incomplete push-off during the stance phase resulting in low values of MPP over the fore-foot. It may be speculated that patients with distal forefoot ulceration especially the hallux and the toes adopt a compensatory strategy of safeguarding the forefoot in an attempt to avoid complete load bearing over the ulcerated area. Such likely variations in the gait cycle due to varied locations of plantar ulceration within the DFU group can account for the low MPP over the forefoot in the DFU group. Pain over the ulcerated area may also contribute to such a gait pattern although it was not investigated in the present study. Even the presence of dressings over the ulcer during the plantar pressure measurement could contribute to the dampening effect resulting in relatively low peak pressures over the total foot area.

Considering all these factors it is reasonable to assume that the peak pressures over the total foot area of the DFU group are sufficiently high to prove as a potential risk for plantar injury.

The next group to be studied was the PFA group, which demonstrated an 11% rise in average MPP over the total foot and a 55% rise in average MPP over the midfoot compared to the DMPN group. The present study demonstrated a significant rise in MPP over the total foot area on the affected limb with the PFA group demonstrating highest average MPP. Despite a 55% rise in average MPP over the midfoot region of the PFA group compared to the DMPN group, the difference between the 3 groups failed to reach a significant level (non-parametric testing) probably due to the small sample size of the PFA group. The DMPN and DFU groups showed comparable values of group means of MPP over the total foot and the midfoot region, whereas the difference in the MPP between the DMPN and the PFA group was clearly evident despite walking at reduced gait velocity. Higher MPP over the total surface area of the amputated foot can be explained by the reduction in the total contact area of the foot during weight-bearing. Whereas the specific 55% rise in average MPP over the midfoot can be explained by the fact that following PFA, the mid-foot assumes the role of the most distal part of the foot in the absence of the fore-foot bearing the brunt of push-off. The peak pressures over the midfoot might have been even higher if the PFA group included all patients with trans-metatarsal amputations (TMA). The combination of TMA with other levels of PFA such as hallux, hallux with toe and ray amputations actually cancelled out the possibly higher MPP values over the midfoot than noticed.

Further classification of the PFA group into subgroups based on the level of PFA demonstrated the variation in the midfoot pressures caused by the level of PFA (refer Table 4.37). Descriptive comparison revealed that the midfoot pressures were highest in patients with TMA amputations, followed by those with hallux amputation and with hallux and toe amputations since loss of the forefoot either completely (TMA) or partially (hallux or hallux with toes) is likely to produce notably high peak pressures over the midfoot during push-off. Whereas the patients with ray amputations presented a picture similar to the DMPN group in terms of the average pressures over the midfoot which barely makes contact with the ground in the presence of an intact fore-foot. As expected the overall reduction in the surface area of the foot due to ray amputation caused a substantial increase in the average total foot pressures compared to the DMPN group.

However, the higher plantar pressures over the midfoot are not surprising following PFA in diabetic neuropathic patients. Higher peak pressures are already documented in patients with PFA on the affected foot (Armstrong & Lavery 1998). It is known that contractures and deformities associated with biomechanical compensation following PFA cause a further increase in plantar pressure, placing an already high-risk limb at further risk for tissue breakdown and re-amputation (Quebedeaux, Lavery & Lavery 1996, Armstrong & Lavery 1998). Patients with trans-metatarsal amputations are reported to be at high risk for skin breakdown (27%) or higher amputation (28%) especially in the first 3 months after the surgery. However, the association of vascular disorders in these patients cannot be overlooked in the understanding of the probable pathways causing re-amputation (Mueller, Allen & Sinacore 1995).

Adaptations in the gait patterns are already known to cause the re-distribution of plantar pressures in diabetic neuropathic patients. Mueller et al. (1994) has shown that compared to using the normal (ankle) strategy, using the hip strategy caused a significant 27% decrease in forefoot and a 24% increase in heel peak plantar pressures. All the patient groups of the present study walked predominantly with an ankle strategy (refer to the net joint moments presented in Table 4.19) causing relatively higher average peak pressures over the fore-foot compared to the heel, (refer to the MPP presented in Table 4.22) regardless of the varied site of ulceration, different levels of PFA and unilateral TTA. Therefore, there is scope for therapeutic reduction of peak pressures by alteration of the gait patterns. However, this area needs further research in these specific diabetic neuropathic patient groups.

Until recently all the research efforts have been focussed on the affected foot of the patients with diabetic foot disease. Therefore, the pressure distribution over the contra-lateral foot of these patients is unclear. In comparison to the contra-lateral foot of the DFU & PFA group, the surviving foot of the TTA group has received some attention.

The results of the present study showed that the peak pressures over the surviving foot in the TTA group were comparable to the pressures over the contra-lateral foot of the DMPN group despite walking 35% slower. Although the peak pressures were not significantly different, it needs to be emphasised that the presence of DMPN in the TTA group is already a risk factor for plantar tissue injury in these patients. The peak plantar pressures over the surviving foot of the diabetic neuropathic amputee patients were compared to the non-diabetic amputee patients previously. The authors confirmed that the higher peak pressures over the surviving foot of the TTA patients with DMPN were due to diabetic neuropathy and not amputation (Veves, Vanross & Boulton 1992). However, in addition to the presence of DMPN, a recent study has pointed out the effect of gait alterations caused by TTA on plantar pressure distribution over the surviving foot (Kanade et al. 2006). This published report was based on the findings of the present study from the part of the data of the DMPN and the TTA groups. The authors reported that despite walking 30% slower compared to the diabetic neuropathic subjects, patients with TTA experienced increased plantar stress on the surviving foot during walking. Adaptations in gait and level of walking activity were identified to affect the plantar pressure distribution and ultimately the risk of ulceration to the surviving foot.

Further to the evaluation of the total surface area of the surviving foot the plantar pressures over specific foot areas is discussed. Regional comparison of the specific foot regions revealed notable difference in the MPP over the heel and the region of 1-2 metatarsals of the contra-lateral foot across the 4 groups. However, the difference was significant only over the heel of the contra-lateral foot demonstrating a rise in MPP from the DMPN to DFU to PFA groups. Although the approach of individual group comparisons was threatened by the consequences of multiple testing, it is interesting to note the pressure pattern over specific foot regions between the 4 groups based on the group means of the MPP. Average MPP was highest on the total foot of the DFU group and over the area of 1-2 MT whereas the PFA group showed highest peak pressures over the heel of the contra-lateral foot. The protective mechanism adopted by the patients with DFU to safeguard the ulcerated foot during walking causes a more pronounced compensatory push-off with the contra-lateral foot which might explain the increase in peak pressures on the contra-lateral foot (refer Table 4.22 and page 249-250 to revisit the protective mechanism adopted by the DFU group).

The adaptations in the gait pattern resulting from PFA can explain the increased plantar stress on the contra-lateral foot. Garbalosa and co-workers have reported significantly greater maximum dynamic dorsiflexion range of motion during walking on the contra lateral ankle compared to the ankle on the affected side following TMA (Garbalosa et al. 1996). Although the present study did not measure the dynamic ankle ROM during the gait, the likelihood of greater dorsiflexion on the contra-lateral foot as noticed by Garbalosa might have resulted in a pronounced heel strike explaining the greater plantar stress on the contra lateral heel of the patients with PFA in the present study. Garbalosa et al. (1996) also noted a similar pattern wherein they found significantly lower pressures over the heel of the amputated foot compared to the forefoot.

As mentioned earlier, although the approach of individual group comparisons was threatened by the consequences of multiple testing; it is interesting to note the pressure pattern over specific foot regions of the contra-lateral foot between the 4 groups based on the average MPP, which demonstrates higher pressures over the contra-lateral fore-foot of the DFU group and the heel region of the contra-lateral foot in the PFA group.

Until now, the pressure distribution over the affected and contra-lateral foot has been discussed in terms of MPP. MPP reflects the absolute peak pressure. However as tissue vulnerability is a factor of both pressure and time, the findings from PTI are discussed hereafter. The relevance of the relationship between pressure-time and skin breakdown has previously been highlighted (Sanders, Goldstein & Leotta 1995). Research has acknowledged the contribution of micro vascular changes to the aetiology of plantar injury along with increased mechanical stress in the presence of DMPN (Cavanagh, Ulbrecht & Caputo 1996). Normally, a pressure of 100mmHg (equivalent to 13.3 kPa) occludes the capillary blood flow (Cavanagh, Ulbrecht & Caputo 1996). Plantar pressures during both standing and walking on normal foot are easily sufficient to occlude capillary blood flow (e.g. plantar pressures in the metatarsal head region are 400 kPa, (Rosenbaum et al. 1994). In case of neuropathic patients a number of local reflexes, including the hyperemic response are modified (Tooke et al. 1987) and this can influence the recovery of vascularity of plantar tissues. It is also suggested that capillary fragility may be greater in people with diabetes (Tooke, Ostergren, Lins & Fagrell 1987). In light of these factors, prolonged weight-bearing can increase the vulnerability of the surviving foot to plantar injury.

In the present study, the PTI decreased significantly over the hallux and the toe regions of the affected foot whereas the heel of the contra-lateral foot showed a significant increase from DMPN to TTA group. The PTI over the hallux was measured only between the DMPN and DFU groups because all the patients with PFA had amputation of the hallux and the TTA group could not be measured for obvious reasons. Therefore, despite walking slower the lower PTI values over the hallux of the DFU group confirm the mechanism of decreased push-off over the ulcerated foot. In case of the toe region the data was missing for the few PFA group patients with toe amputations and all the patients with TTA. Therefore, the significant decline from DMPN to PFA group could be as a result of an artefact.

However, the steady increase in the PTI over the heel of the contra-lateral foot adds to the already increased risk of plantar injury to the total contra-lateral foot from notably higher average MPP of the DFU group.

After discussing the instantaneous plantar pressure distribution, it is now important to consider the added effect of the volume of walking over a day on the cumulative plantar stress. The present findings demonstrate significant variation and decline in the DPCS over the hallux and the toes of the affected foot across the three groups. On the contra-lateral foot, the 3-4-5 MT region showed a significant decline in DPCS across the groups.

It has been established that moderate repetitive stress is equally instrumental in the causation of plantar ulceration (Bauman & Brand 1963, Bauman, Girling & Brand 1963) as much as high pressures. Although the likely influence of the level of weight bearing activity on the mechanical trauma accumulated by plantar tissues among individuals with diabetes was identified since long, (Cavanagh, Ulbrecht & Caputo 1996) the concept of cumulative plantar stress was explored only recently. It was proposed that the tissues atrophy and become weaker in response to chronically low levels of stress (Mueller & Maluf 2002). Maluf & Mueller (2003) studied daily weight-bearing activity and cumulative plantar tissue stress in subjects with DMPN. They demonstrated that subjects with DMPN and a history of recurrent plantar ulcers are less active than subjects without DM and accumulate lesser plantar tissue stress per day than subjects with and without DMPN who had never developed a plantar ulcer (Maluf & Mueller 2003). These findings suggest that plantar tissues may be more susceptible to injury at relatively low levels of cumulative stress following an initial episode of skin breakdown.

The findings from the present study contribute to the existing literature by adding the results from patients with current ulceration, partial foot amputations and trans-tibial amputations. The patients with TTA experience the least cumulative stress followed by the patients with PFA, DFU and DMPN. As per the principles of the Physical Stress Theory, the patients with TTA should be maximally prone to plantar ulceration among the four groups. However, it may be argued that the patients with TTA accumulate less plantar stress because of decreased volume of daily walking. Most recent evidence regarding DPCS suggests that plantar tissue injury may result from sudden changes in activity and the routine loading of plantar tissues rather than an absolute value of peak plantar pressure or step count (Lott, Maluf, Sinacore & Mueller 2005). The authors reported in the case history that the patient demonstrated peak plantar pressure well below his recommended threshold while wearing the AFO on the day of ulceration. Whereas he experienced an increase of more than 300% in the amount of cumulative plantar stress on the day of ulceration compared to the other days of activity monitoring which is speculated to be dominated by the rapid change in the number of steps rather than the total number of steps.

Evidence from all the above studies imply that either the complex mechanism of plantar injury from cumulative stress is still not clear or it can be inferred that plantar injury resulting from cumulative stress can occur from two causes. The mechanical trauma to the tissues from sudden change in the level of activity is equally responsible as much as the chronically low levels of plantar stress from reduced daily walking. The second inference is in tune with the Physical Stress Theory, which proposes that extreme deviations from the maintenance stress range that exceeds the capacity of tissue result in tissue injury (Mueller & Maluf 2002).

Summary: To summarise it needs to be emphasised that the diabetic neuropathic population is already at risk of plantar injury due to the presence of neuropathy. The significantly higher total foot pressures noticed with the progression of further foot complications despite a significant reduction in gait velocity and rise in the severity of neuropathy suggests an increasing risk of plantar injury to the affected foot from the DMPN to DFU to PFA group. In the present study, the total foot pressures are more indicative of the risk of plantar injury than the specific plantar areas because of the heterogenous nature of the DFU and the PFA groups in terms of the site of plantar ulceration and the level of foot amputation respectively.

Irrespective of the site of ulceration or the level of PFA or the occurrence of TTA, all the patients walked with a predominant ankle strategy demonstrating relatively higher average peak pressures over the fore-foot compared to the heel. However, the specific effect of DFU and PFA was evident in the gait alterations produced at the ankle joint on the affected and the contra-lateral limbs.

The averaging effect of the peak pressures due to different sites of plantar ulceration, the tendency to safeguard the ulcerated foot, the decreased gait velocity and the inefficient push-off of the ulcerated foot, all contributed towards the relatively less peak pressures over the affected forefoot of the DFU group than would be expected in comparison to the results of the previous studies. However, the total affected foot pressures of the DFU group were significantly higher than the DMPN group indicating greater risk of plantar injury. The relatively pronounced push-off on the contra-lateral limb to compensate for the inefficiency on the affected side the DFU group contributed to the higher average MPP and PTI over the contra-lateral forefoot indicating an increased risk of plantar injury to the contra-lateral forefoot in particular.

The PFA group demonstrated highest peak pressures over the total affected foot due to the obvious reduction in the total contact area of the foot during weight-bearing. On the contra-lateral limb, the likelihood of greater dynamic dorsiflexion of the contra-lateral ankle during gait might have resulted in a pronounced heel strike explaining the greater plantar stress on the contra lateral heel of the patients with PFA compared to the remaining 3 groups.

In case of the TTA group, the heel region of the surviving foot demonstrated an increased risk of plantar injury indicated by the significantly high PTI over the heel probably due to the significantly decreased gait velocity and prolonged heel strike on the contra-lateral limb in an attempt to compensate for the inefficient heel strike on the prosthetic limb.

Based on the findings of the present study it can be inferred that the specific area at risk on the affected foot is the fore-foot in the DFU. However, on the contra-lateral foot, in addition to the total surface area of the foot it is the heel in the PFA and TTA group and the forefoot in the DFU group which is at risk of plantar injury.

It also needs to be noted that irrespective of the cumulative level (volume) of walking activity, the plantar stress produced by a dynamic activity such as walking in itself produces a level of stress that is threatening to the plantar tissues. The plantar stress (foot pressures) produced by walking is comparable to other daily ambulatory activities (Maluf, Morley, Richter, Klaesner & Mueller 2004) and therefore appropriate protection of the diabetic neuropathic foot on the affected and contra-lateral limb during walking is mandatory to prevent further risk of injury in this patient group.

5.5: Activity level:

5.5A: Capacity of walking:

The domain of activity was studied based on its two constructs: capacity and performance. Therefore, both capacity and performance of walking was evaluated to grade the level of walking in this patient population. Capacity is discussed before the performance of walking in this chapter.

It is established that the interruption of normal gait cycle and the energy conserving characteristics of the trunk and limb motion results in increased energy expenditure (Waters et al. 1999). Nevertheless, it has been postulated that in response to a gait disability the patient will adapt by performing compensatory gait substitutions to minimize the additional energy expenditure (Inman, Ralston & Todd 1981). The findings from the present study demonstrate that the energy expenditure of the diabetic neuropathic patients increases with consequent stages of foot complications. It needs to be highlighted that these results reflect the level of energy expenditure at their customary walking speed in the presence of the adaptations produced in gait as a result of diabetic foot complications. Additionally it needs to be specified that none of the participants presented with active clinical manifestations of cardio-vascular or respiratory disease since the presence of either disorder would have influenced their energy expenditure (Grazzini et al. 2005). However, the extent of influence of cardio-respiratory disorder which is clinically stable is unclear. There was a scattered distribution of patients with history of cardiac or respiratory disorders between the 4 groups who were clinically stable during the assessment (refer Table 4.3).

Considering the multi-system nature of involvement of DM, it would be impossible in practice to recruit patients with no history of cardiac or respiratory disorders. Therefore controlling for current manifestation of cardio-respiratory disorders was the most stringent strategy that could have been adopted to reduce the bias in the interpretation of the results. Additionally the present study sample closely resembles the general diabetic neuropathic patients, which face multisystem problems.

The 4 groups demonstrated a significant difference in their energy expenditure during walking. A significantly steady rise was noted in the score of THBI indicating increased energy expenditure as the patients moved from DMPN to DFU to PFA to TTA. However, specific group comparisons did not reveal significant differences between the DFU vs. PFA groups and PFA vs. TTA groups.

Descriptive comparison of the diabetic neuropathic groups with healthy non-diabetic subjects demonstrated that the mean value of the DMPN group was very close to the mean THBI score of the healthy non-diabetic subjects. It was interesting to note that the THBI score of the young healthy non-diabetic subjects was comparable to the score of the elderly diabetic neuropathic subjects. Such an observation can be explained in two ways. Firstly, the different methods of measurement between the two studies could mask the actual differences in the results. Secondly, it may be reasonable to argue that the gait deviations produced by diabetic neuropathy alone might not be significant to cause remarkable difference in the energy expenditure of these patients in walking. In the similar context, it may be interesting to conduct further research to compare diabetic patients with and without peripheral neuropathy to investigate the exclusive effect of diabetes neuropathy on the energy expenditure.

However, the transition from diabetic neuropathy to plantar ulceration to PFA to TTA clearly indicates a decline in the capacity of walking in diabetic neuropathic patients. In the first instance, it may appear that, the presence of active plantar ulceration may increase the energy expenditure due to i) the deviations produced in the gait pattern or ii) the systemic changes occurring in the body in response to tissue damage or iii) a result of instructions to decrease the physical activity during the period of wound healing or iv) a combination of all the three factors. Analysis of a detailed metabolic profile of the diabetic neuropathic patients during the phase of healing of the ulcer would be necessary to explore the systemic influence on the energy expenditure during walking. Such a thought could provide the basis for a more detailed study in the future to address this specific research question since the present study is limited in discussing the interplay of systemic factors and their influence on energy expenditure.

At this stage, it would be appropriate to highlight that the present study included relatively more Type 2 DM patients in the ulcer group compared to the Type 1 DM. It has been reported that low cardio respiratory fitness and physical inactivity are independent predictors of all-cause mortality in men with Type 2 DM (Wei et al. 2000). In the light of lack of evidence suggesting decreased physical capacity in Type 2 DM patients compared to Type 1 DM and the relatively small number of patients in the each group of the present study it may be difficult to associate the type of DM with decreased physical capacity in patients with DFU.

However, the results of gait analysis allow evaluation of the impact of gait alterations on the capacity of walking. It is evident from the results of the gait analysis that plantar ulceration did not cause major alterations in the gait cycle. The inefficient push-off on the affected limb did not require major compensatory changes in the gait pattern. Although the biomechanical restraints caused by plantar ulceration have not been evaluated previously in terms of energy expenditure during walking, researchers have investigated the effect of ankle fusion on energy expenditure. Waters & Mulroy (1999) reported a 3% greater energy expenditure for an average person with ankle fusion compared to a normal subject walking at the same speed. Therefore, it appears less likely that the gait deviations following plantar ulceration can play a major role in increasing the energy expenditure by 21 % compared to the diabetic neuropathic subjects. Rather the more influential factor could be the prolonged period of decreased physical activity due to the longer period of ulcer healing. Although the patients were not followed up until the ulcers healed, the average onset period of ulceration was 13.4 months in the present study. Even a previous study has reported the duration of ulcer to be 8.8 months when the patients entered the trial for wound dressings (Ahroni, Boyko & Pecoraro 1993). Such a prolonged period appears to be a substantial length of time duration to decrease the physical capacity of a diabetic patient whose physical activity is curbed due to an active plantar ulcer.

Patients with PFA showed a further rise in energy expenditure compared to the DFU group. Parallel to the previous discussion (previous paragraph) regarding the gait alterations caused by ankle fusion and its impact on energy expenditure it seems unlikely that the gait deviations alone would contribute to a 34 % rise in energy expenditure. However, the extensive period of decreased physical activity from the point of time of ulcer occurrence to the point of healing of the surgical wound following PFA can contribute a great deal to the rise in energy expenditure. Larsson et al. (1998) reported an average healing time of 29 weeks, range 3-191 wks for a minor amputation (below the ankle) in diabetic patients (Larsson, Agardh, Apelqvist & Stenstrom 1998). Generally, infected, gangrenous non-healing ulcers are an indication for PFA in diabetic patients (Mckittrick, Mckittrick & Risley 1993). It seems reasonable to presume that various non-surgical therapeutic measures would have been tried to aid the healing process before the amputation surgery. Although there is no documented threshold to determine the minimal length of time needed to produce the effects of deconditioning after refraining from walking, restricted or limited level of physical activity for a prolonged period such as 29 weeks appears to be a sufficiently long time period to produce an effect of deconditioning in these patients.

Lack of attention to the physical fitness of the diabetic patient during this period until the healing of the surgical wound and lack of rehabilitation to improve the level of fitness after the healing of the surgical wound following PFA can deteriorate the capacity to walk in this group of patients.

The TTA group demonstrated the highest level of energy expenditure among the 4 diabetic neuropathic groups. The TTA group demonstrated a 38% rise in energy expenditure compared to their able-bodied diabetic neuropathic patients. This finding is not surprising considering the loss of ankle-foot complex, which is known to increase the energy expenditure during walking because the loss of power from the ankle plantar flexor muscles is substituted by the increased acitivity of the large muscles for e.g. hip and knee muscles (Torburn et al. 1990, Powers et al. 1996). Patients with non-vascular TTA (22-75 yrs age) showed a 20% elevation of rate of oxygen consumption over that of the younger control subjects (Gailey et al. 1994). The demand placed by the loss of ankle power poses a greater challenge for the older diabetic patient with multi-system involvement of the disease although the patients were free of any active clinical manifestations of cardio-respiratory disorders. The use of the prosthesis itself increases the energy demands during walking due to the utilization of the remaining proximal muscles, which are large group muscles around the hip and the knee to substitute for the loss of the small group muscles around the ankle following TTA.

In addition to evaluating the effect of the further foot complications the probable effect of smoking was also considered in the entire discussion since smoking is known to be associated with decreased aerobic capacity (Tchissambou et al. 2004). However, the present study included a relatively small number of patients smoking (3 patients per group on an average). Moreover, the distribution of the patients smoking was fairly similar between the four groups ruling out the likely bias of smoking on the energy expenditure of the patients.

To summarise, the present results confirm the decline in the level of physical fitness demonstrated by increased energy expenditure across the four groups (Figure 4.18). Alternatively, it could be argued that walking requires more physical exertion (in terms of aerobic capacity) as the level of physical impairment progresses. Therefore, the level of physical fitness and the level of physical impairment are interdependent. It is hard to establish a cause-effect relationship between these two factors without making use of a longitudinal study. Irrespectively, the steady rise in the energy expenditure indicates the greater need for improving the level of fitness as the diabetic patient's progress from peripheral neuropathy to foot ulceration to minor amputations to major amputations of the lower extremity.

However prior to making any recommendations to clinical practice regarding the therapeutic measures to improve the physical fitness in the diabetic neuropathic patients with consequent stages of foot complications, it is necessary to consider their actual performance of walking activity.

5.5B: Performance of walking:

Average daily strides were used as a measure to indicate their daily walking performance. The four groups walked significantly different demonstrating a significant overall decline in their performance from DMPN to TTA groups with the exception that the PFA group demonstrated a marginally higher mean value of average daily strides compared to patients with DFU.

Specific group comparisons revealed a significantly low daily walking performance of the TTA group compared to the PFA group. However, the comparison between the DFU and PFA groups did not reveal significant differences.

Based on the speculation that age may have a likely influence on the walking performance the association between age and daily walking was examined. In the light of the evidence that older patients (50+ yrs) demonstrate reduced aerobic capacity (Gall & Parkhouse 2004) it would be expected that the walking performance declined with increasing age. However, it was interesting to note that the present results did not reveal significant correlation between the two variables. There could be several reasons for such an observation. Unlike the healthy subjects who may walk as much as they can walk, the diabetic neuropathic patients with foot complications probably walk only as much as they need to walk. The healthy subjects may not feel restricted and may actually vary their activity depending on what they want to do, whereas the people with DM might restrict themselves to essential activities i.e. drop any luxury in terms of walking activity.

It has been documented previously that patients with neurological disease have a reduced ability to vary their activity level probably due to the wide range of neurological/behavioural impairments (Busse, Pearson, van Deursen & Wiles 2004). Similarly, the physical limitations caused by the diabetic foot complications may lead to an approach towards daily activity, which is governed by what they can do rather than what they want to do or are required to do at a particular age. Such an approach towards daily activity can cancel out the likely influence of age on the walking performance of diabetic patients with foot complications. Moreover it has been demonstrated earlier that physical activity declined minimally only after the age of 75 yrs among older people (Fone & Lundgren-Lindquist 2003). Had the present study included patients above 75 yrs the likely influence of age on walking performance may have become evident but the cut-off age for the present study being 75 yrs may explain the lack of association.

Descriptive comparison of the results from the diabetic neuropathic patient groups with the non-diabetic healthy subjects demonstrated that the DMPN group showed a low value of average daily strides compared to the non-diabetic healthy subjects. Although the DMPN group did not present with any mechanical disruption of the plantar tissues or anatomical loss of the part of the feet, they demonstrated decreased average daily walking performance compared to the non-diabetic healthy subjects. It is speculated that the overall influence of the multi-system involvement of the disease itself and the specific influence of the impaired sensory feedback from the feet, altered balance in standing and decreased gait velocity can attribute to the 30.9% decrease in average daily strides compared to the healthy subjects. However further investigation in this area would be necessary to confirm this speculation.

Patients with DFU showed a further reduction in their walking performance compared to the DMPN group. The effect of plantar ulceration on daily walking was clearly evident over and above the existing sensory neuropathy, decreased stability in standing and gait velocity in these patients. However, the implications of plantar ulceration on daily walking performance can be several. Patients with DFU may have walked less due to their own conscious attempt to refrain from walking or in an attempt to comply with the instructions of the treating foot care team to allow healing of the plantar ulcer or due to decreased physical capacity to walk as indicated by higher energy expenditure compared to the DMPN group. The majority of patients with plantar ulceration (n=12/23, i.e. 52.2 %) were instructed to walk as much as necessary for ADL, whereas some (n=8/23, i.e. 34.8%) patients received no instructions pertaining to the walking activity from the foot care team. Two patients were instructed to not walk at all, whereas one patient received confusing instructions: no walking at all from the district nurse and walking as much as necessary for ADL from the specialist clinic. Therefore, the effect of compliance to the walking related instruction on daily walking performance cannot be overlooked.

Descriptive analysis of the average daily strides of the subgroups classified as per walking instruction may provide some insight in this discussion (refer Table 4.38).

Further sub-classification of these patients based on the instruction received regarding daily walking demonstrated that patients who were instructed to walk only as much as necessary for daily activities actually walked less (1016 strides less) compared to patients who received no instructions regarding walking activity. Additionally, the average value of the total DFU group (n=23) was close to the average value of the sub group of patients, who received no instructions regarding their walking activity, which raises the following question. Whether the actual mean of average daily walking of the entire group might have been less if all the patients were instructed similarly i.e. to walk only as much as needed for ADL. In that case, the average daily strides of the DFU group might have been similar to the TTA group (1894 strides). It was interesting to note that patients who were instructed to offload the foot completely walked almost twice the number of daily strides (5244 strides) compared to the patients who were instructed to walk only as much as needed for ADL (2538 strides).

The area of adherence to walking instructions and the actual performance of walking is complex and involve many factors such as the facilities available to comply with the instruction, the beliefs about the process of healing and its relation to walking, the level of education of the patients regarding this issue and the socio-economic conditions of the patients. Descriptive sub-group analysis of the DFU group of the present study can only indicate that the actual performance of daily walking of the patients with DFU may have been actually less than the average of the total DFU group presented in the study. However, this area needs further investigation.

Secondly, it is hard to speculate whether the decreased physical capacity caused the reduction in walking performance of the DFU group or whether the walking performance was merely a direct reflection of the actual reduction in the walking activity during the period of ulcer healing. Although the DFU group was not followed up until the point of ulcer healing, the average onset period of ulceration was noted to be 13.4 months in these patients. Even a previous study has reported the duration of ulcer to be 8.8 months when the patients entered the trial for wound dressings (Ahroni, Boyko & Pecoraro 1993). Although there is no threshold documented to determine the length of time needed to produce the effects of deconditioning after refraining from walking, restricted or limited level of physical activity for a prolonged period such as 13.4 months appears to be a sufficiently long period to produce an effect of deconditioning in these patients. To investigate the precise cause-effect relationship between capacity and performance of walking in this patient group, a longitudinal study would be necessary.

Partial foot amputation also appeared to demonstrate its effect on walking performance. The PFA group walked 29% less compared to DMPN group. It is necessary to highlight at this stage that all the patients in this group had healed PFA. Although it is not documented, it is reasonable to expect that the presence of a non-healed surgical wound following foot amputation would further restrict the walking activity of the patient with PFA. In the absence of such likely attempts to curb the walking activity deliberately, their performance can be considered as the true reflection of their physical capacity and biomechanical alterations produced due to unilateral diabetic foot amputations. The decreased physical capacity is indicated by significant decline in the energy expenditure across the four groups ($p=0.002$). The increased biomechanical challenges are indicated by the significant decline in gait velocity ($p<0.001$), standing balance ($p=0.002$) across the 4 groups and the significantly decreased peak plantar flexor moments at the affected ankle ($p=0.003$) compared to the DFU group indicating a decreased push-off during walking.

The next group studied was that of TTA. Patients with TTA walked the least between the four groups. A significant decline of 57.1% in the walking performance of the TTA group compared to the DMPN group demonstrates the notable negative impact of major amputation on the level of physical activity. More than 50% reduction in physical activity in these patients can be attributed to decreased physical capacity (aerobic capacity-38% increase in energy expenditure compared to DMPN) and the established biomechanical alterations in the gait cycle. The significant reduction of 39.8% in walking performance of the TTA group compared to the PFA group also demonstrates the challenges posed by major amputations compared to minor lower extremity amputations in terms of gait alterations, energy expenditure and functional independence (Waters, Perry, Antonelli & Hislop 1976, Garbalosa, Cavanagh, Wu, Ulbrecht, Becker, Alexander & Campbell 1996, Hosch, Quiroga, Bosma, Peters, Armstrong & Lavery 1997).

The overall decline in daily walking performance with progression of foot complications from DMPN to TTA is significant. However the graph related to the significant linear polynomial contrast between the groups demonstrates that, the patients with PFA walked more than the patients with DFU (refer Figure 4.21). There is a possibility that an apparently marginal difference of 2.8% between the average values of the DFU and PFA groups may become evident in a larger study with greater number of subjects. However, the overall decline in walking performance is in tune with the pattern noticed by Tennvall & Apelqvist (2000) in the H-R QOL among diabetic people at different stages of foot complications (Tennvall & Apelqvist 2000). Diabetic patients with minor amputations are reported to demonstrate better H-RQOL compared to patients with current ulcers and patients with major amputations are reported to demonstrate lower H-RQOL compared to patients with minor amputations (refer to the section on H-RQOL in this chapter for in depth discussion on this topic). Although no direct evidence was located to support the linear relationship between the volume of walking activity and H-RQOL, it may be reasonable to expect that walking may have a positive influence on the H-RQOL of the individual. Further research in this area would be necessary to explore this relationship.

5.5C: Summary of the capacity and performance of walking:

Based on the findings from the two constructs of walking activity the present study demonstrates that there was a decline in the level of activity at consequent stages of foot complications. The neuropathic group without further foot complications demonstrated the highest level whereas the TTA group demonstrated the lowest level of activity. The group with minor amputations i.e. PFA performed better than the group with major amputations i.e. TTA. The seemingly better performance of the PFA group compared to the DFU group is open to various speculations regarding the cause for such a finding.

It is hard to interpret whether the decreased physical capacity caused the decreased performance of walking in the DFU group or whether the actually decreased walking activity during the prolonged period of ulcer healing led to decreased walking performance of this group. However, it was interesting to note that the walking performance of the DFU group was similar to the PFA group although there was further decline in the energy expenditure of the PFA group compared to the DFU group. Such an observation supports the argument that probably the DFU group has a better capacity to walk but are limited in walking because of the conscious attempt to safeguard the ulcer. Irrespective of whether decreased capacity caused decreased performance or decreased performance caused decreased capacity it is evident that the increasing level of physical impairment leads to a deterioration in the level of activity.

The group with minor amputations i.e. PFA performed better than the group with major amputations i.e. TTA. However, it is necessary to highlight that PFA still produces a 34% rise in energy expenditure compared to patients with DMPN. Such a finding emphasises the fact that although there is a conscious attempt to salvage the foot for ambulation, (Sanders & Dunlap 1992) lack of rehabilitation following foot amputations in diabetic people may result in substantial reduction in the capacity to perform an activity, effectively decreasing their level of activity in daily life. Merely saving the maximal length of the limb may not promise a maximal level of functional independence as intended.

5.6: Participation: H-RQOL:

H-RQOL in the 4 groups of patients was assessed using a generic tool: SF-36 and a condition specific tool i.e. Cardiff Wound Impact Scale. The results obtained from the two measures are interpreted separately prior to a comprehensive discussion of H-R QOL based on the findings from both tools.

5.6A: SF-36:

The findings from the present study demonstrate a significant difference in physical function, role limitation due to physical problems and social function between the 4 groups. There was a significantly steady decline in physical function and their role limitation due to physical problems across the groups from DMPN to TTA demonstrating a relatively larger reduction from DMPN to DFU (18.81%) and PFA to TTA (29.77%) compared to the difference between the DFU and PFA groups (11.78%). Specific group comparisons did not reveal significant differences between DFU vs. PFA and PFA vs. TTA groups in any of the domains of SF-36 health profile.

Several studies have evaluated H-RQOL of diabetic patients using the SF-36 (Gulliford & Mahabir 1999, Ahroni & Boyko 2000, Davies et al. 2000, Nabuurs-Franssen, Huijberts, Kruseman, Willems, & Schaper 2005). It has been observed that neuropathic complications along with renal complications are known to have the greatest effects on SF-36 scores

(Ahroni & Boyko 2000). Among the various domains of H-RQOL, the peripheral nerve picture is known to be strictly related to the physical aspects of the patients' quality of life, and not with the mental aspects (Padua et al. 2001). The findings of the present study concur with the previous results demonstrating a significant variation in physical function and role limitation due to physical function along with a decline in physical function across the four groups from DMPN to DFU to PFA to TTA.

Based on the results from the present study and previous reports it can be confirmed that patients with current plantar ulceration appear to have poor H-RQOL compared to their diabetic counterparts without prior foot ulceration and patients with a healed foot ulcer (Tennvall & Apelqvist 2000, Nabuurs-Franssen, Huijberts, Kruseman, Willems & Schaper 2005). It has also been observed that the healing of a foot ulcer resulted in a marked improvement of several SF-36 subscales 3 months after healing and HRQOL declined progressively when the ulcer did not heal (Nabuurs-Franssen, Huijberts, Kruseman, Willems & Schaper 2005). Such an observation confirms the negative impact of DFU on H-RQOL.

The decline in physical function on SF-36 is in tune with the self-reported decline in mobility on the RMI and the decline in average daily walking of patients with DFU compared to the DMPN group. Such an observation indicates that there appears to be an agreement between the patients own perception of physical function and their performance measured in terms of physical function. As rightly pointed out by Price (2004) the enormous impact of lack of mobility in everyday living for both the patient with ulceration and his or her caregivers led Brod (1998) to refer to the condition as “the burden of a non-weight-bearing” regimen.

In addition to the decline in physical function, patients with foot ulcers have also demonstrated decreased emotional and social function (Reiber, Lipsky & Gibbons 1998). The emotional function is not only reduced in the patient but a diabetic foot ulcer is known to be a large emotional burden on the patients' caregivers as well (Nabuurs-Franssen, Huijberts, Kruseman, Willems & Schaper 2005). Even in the present study, the DFU group scored the least on their role limitation due to emotional problems among the 4 groups (34.8% less than the DMPN group). The association of the ulcers with daily dressing changes, trips to health care providers, topical or systemic medications and the anxiety about the outcome (Price 2004) can explain their role limitation due to emotional problems. However, there was no significant difference in the score for their role limitation due to emotional problems between the 4 groups in the present study. Neither was the mental health score between the 4 groups different.

The present findings also demonstrate that the DFU group presented the least average score (34.3% less compared to the DMPN) on social function between the 4 groups. The difference between the 4 groups was significant although there was no evident trend across the groups. Even previous studies have reported that the existing or previous foot ulcer causes a negative impact on the social function as reported by the patients (Reiber, Lipsky & Gibbons 1998, Meijer et al. 2001). It is possible that the presence of odour or the leakage from the wounds may discourage diabetic patients with foot ulceration from social participation.

The mean score of social function in the PFA group was higher than the DFU group indicating that although the physical impairment due to PFA may be more severe than plantar ulceration the above mentioned factors associated with wounds may inhibit the

DFU group patients from social participation. However, specific comparison between the two groups did not reveal significant differences in social function nor physical function. Despite a 27.4% difference in the group means the non-significant difference between the two groups may be attributed to small number of patients in each group. Secondly, the present study was not powered to detect the differences on the SF-36 as this was a secondary objective of the study.

The present findings are in tune with previous studies, which report that diabetic patients with minor amputations are reported to demonstrate better H-RQOL compared to patients with current ulcers (Tennvall & Apelqvist 2000) and mobile amputees are known to present with better psychological status when compared to subjects with a diabetic foot ulcer (Carrington, Mawdsley, Morley, Kincey & Boulton 1996). Although it has not been tested, it may be reasonable to expect that better psychological status can exert a positive influence on the social function of the patients with PFA. Diabetic patients with foot ulceration are reported to be more depressed and dissatisfied with their personal lives compared to diabetic patients with no history of foot complications (Carrington, Mawdsley, Morley, Kincey & Boulton 1996). In addition, it is reasonable to expect that the amputee patients who are mobile must be more motivated compared to the patients with DFU who are reported to be depressed and dissatisfied with their personal lives. Such a mental state of depression and dissatisfaction can contribute to their lack of motivation to paticipate in social function. A previous study has already confirmed the impact of anxiety, depression and negative beliefs about illness on the mental functioning of the diabetic patients (Paschalides et al. 2004).

Compared to the DFU group, patients with PFA demonstrated a further reduction in the physical aspects of H-RQOL. Based on the average score of physical function and significant linear contrast across the 4 groups (refer Table 4.29), the patients with PFA perceived severe limitation in physical aspects of H-RQOL compared to the DMPN and DFU groups. The perception of increasing physical demands caused by the PFA on tasks such as STS, balance in the standing posture, walking and the increase in energy expenditure during walking can explain the further reduction in physical function of these patients.

Patients with TTA demonstrated the lowest score on the scale of physical function confirmed by the significant decline across the 4 groups. The overall decline in the H-RQOL in the physical aspect from DMPN to TTA in the present study clearly indicates that the patients also perceived a decline in the physical aspect of their H-RQOL with progression of physical impairment from DMPN alone to TTA. Such an observation is parallel to the results from a previous study, which demonstrates SF-36 to be responsive to the development of diabetic complications over time (average 3.1 yrs) among the elderly people (Ahroni & Boyko 2000). Based on the trend observed in the present study and the previous evidence it is reasonable to presume that if the findings of the present cross-sectional study were to be extrapolated over (time) a longitudinal clinical scenario (study), patients with DMPN would demonstrate a decline in the physical aspect of the H-RQOL with progression of foot complications.

Major lower limb amputations are already known to significantly reduce HRQOL (Tennvall & Apelqvist 2000). They are known to have a significantly higher impairment in the physical dimension compared to diabetic patients without amputations (Peters et al.

2001). The substantial deterioration in performance of the various mobility tasks such as STS transfer, balance in standing posture and the reduction in the capacity and performance of walking activity can contribute to the patient's perception of decline in the physical function following TTA. However, their mental health was comparable to the remaining 3 groups showing no significant difference between the four groups.

Peters et al. (2001) documented a similar observation that there was no significant difference between the psychosocial functional level of diabetic patients with unilateral amputation and diabetic patients without amputations (Peters, Childs, Wunderlich, Harkless, Armstrong & Lavery 2001). Since all the 4 groups in the present study presented with loss of protective sensation over the feet from diabetic neuropathy, such an observation may be due to the factors surrounding the perception of one's limb. It is believed that in the absence of sensation, a patient may "psychologically disown" one's limb well before any inciting event precipitates amputation (Brand 1983, Brand 1991). Secondly, it may be a result of the patients control over their physical disability. Over time, patients might cope with their physical limitations and alter their functional expectations (Deyo et al. 1982). Such a mental attitude may lead to lack of difference in the mental health of the 4 groups which are at progressive stages of foot complications and demonstrate a significant difference in their level of capacity and performance of daily activity for e.g. walking.

Although no study has previously attempted to compare the four diabetic patient groups at consequent stages of foot complications there is evidence to suggest that patients with major amputations are reported to demonstrate lower H-RQOL compared to patients with minor amputations and patients who healed primarily without any previous amputation

(Tennvall & Apelqvist 2000). However, it was interesting to note that even the patients with major LEA (TTA) demonstrated a mean value of social function, which was comparable to the mean of the DFU group in the present study. Despite a reduction of 38.05% in the average physical function score of the TTA group compared to the DFU group the average social function score of the 2 groups was comparable (DFU group=53.44 & TTA group=58.08). Such an observation warrants the need for standardised data in diabetic population to investigate whether only a certain minimal level of physical function is necessary to perform social function and whether physical function is directly associated with social function.

In terms of the remaining domains of SF-36 namely vitality score, bodily pain, general health perception and change in health status, the present study failed to reveal any significant differences between the four groups. However a previous study has demonstrated the association between the appearance of any neuropathy complication and a decline in general health and vitality score of SF-36 in diabetic patients (Ahroni & Boyko 2000).

The two domains of SF-36 namely- the Physical Function and the Role limitation due to physical problems which showed significant declines from DMPN to TTA were examined for the possibility of a floor effect within the 4 groups separately to check whether the SF-36 score underestimated their performance in these two domains. It was interesting to note that there was a rise in the number of patients scoring less than 20% in the domains of Physical function and Role limitation due to physical problems from the DMPN to TTA group. Such an observation indicates that with the progression of the physical impairment there was a greater possibility of the actual H-RQOL been worse than it was measured by the SF-36 in the aspect of Physical function (especially in the TTA group) and the domain of Role limitation due to physical problems. However, it was interesting to note that there were more patients with DFU compared to PFA suggesting that the Role limitation due to physical problems could have been actually worse than measured by SF-36 in patients with DFU compared to patients with PFA in this domain.

Therefore, it can be inferred that the floor effect may have affected the sensitivity of the tool to identify the actual degree of clinical change across the 4 groups. Further investigation with larger sample size is necessary to repeat such a study to detect the actual degree of clinical change in H-RQOL of these patients especially in the domains of Physical function and Role limitation due to physical problems.

Results from the secondary analysis demonstrated that the comparison between minor amputations (PFA) and major amputations (TTA) did not reveal significant differences in any domains of SF-36. Non-significant differences between the two groups may be because of the inadequate sample size required to detect a minimum of 20-point difference on the 100-point scale of SF-36 score (Ware, Snow, Kosinki & Gandek 1993). A 20-point difference on the scale was considered significant for the present study. Although researchers in the field of Quality of life would consider even a difference of 5 to 10 point significant for H-RQOL data, 20-point difference was considered significant. Because it is fairly standard to consider a 20% difference in clinical trials. Secondly, the sample size of the individual groups in the the present study was close to that recommended by Ware et al. (1993) to detect a 20 point difference when two experimental groups are compared (Ware 1993). The sample size of the present study was estimated to detect differences in the average gait variables between the four groups rather than the SF-36 scores.

To summarise the findings from SF-36, the results from the present study indicate a decline in physical aspects of functional health status across the four diabetic neuropathic groups with progression of foot complications. With the progression of physical impairment there was a greater possibility of the actual H-RQOL being worse than it was measured by the SF-36 in the aspect of Physical function (especially in the TTA group) and the domain of Role limitation due to physical problems. The floor effect might have reduced the sensitivity of the tool to identify true degree of clinical change across the 4 groups in terms of Physical function and Role limitation due to physical problems.

Although the Social Function was significantly different between the 4 groups there was no particular trend observed across groups. Although non-significant, the apparently better performance of the PFA group than the DFU group in Social Function is in line with previous findings, which suggests that patients with healed minor amputations of the lower extremity present better psychological status and H-RQOL compared to patients with active foot ulceration. The patients with TTA present with poorer H-RQOL compared to the DMPN, DFU and PFA groups in the physical aspect.

5.6B: CWIS:

The overall trend in Physical and Social Function across the 4 groups was similar on the CWIS as the respective SF-36 scales. This observation is not surprising, as these scales in CWIS have been correlated with the respective scales of SF-36 previously to test the construct validity of the CWIS. The researchers noted significant correlations between the respective scales of physical and social function of the two tools. The Well-Being scale of

CWIS correlated with the mental health and role limitation due to emotional problems measured by SF-36 (Price & Harding 2004).

The domain of Physical Symptoms and Everyday Living scored by CWIS focussed on the impact of symptoms on daily functioning and comfort. The four groups varied significantly in their Physical Symptoms and Everyday Living demonstrating a significant decline from the DMPN to the TTA group. The DMPN group scored the maximum and the TTA group scored least; however, no floor effect was noticed in this domain. The DFU and the PFA groups presented with similar scores.

The trend observed in Social Life was very similar to the pattern of Social Function reported using the SF-36 between the 4 groups. All 4 groups varied significantly in their Social Life, however there was no significant trend across them. The DMPN group scored the maximum followed by the PFA group followed by the DFU and TTA groups, which scored similar. The CWIS demonstrated better average score (17.8%) of Social Life in the PFA group compared to the DFU group for reasons explained earlier (refer page 251-252). However, specific group comparison between DFU vs. PFA did not reveal any significant variations.

The domain of Well-Being was measured only in the DFU group and therefore could not be compared to the other groups within the present study. However, the average well-being score from the DFU group of the present study was compared to the average score from a group of 89 patients with non-healed ulcer (Price & Harding 2004). Although this group of 89 patients was a mixture of patients with diabetic foot ulcer and chronic leg ulcers their mean score (38.7) was not very different from the DFU mean score in the present study

(36.7). This similar score suggests the impact of a lower extremity ulcer on the self-reported well-being of the patient is similar irrespective of the cause of the ulcer. Whether diabetic foot ulceration has any exclusive impact on the well-being of the patients needs further investigation.

It was interesting to note that there was no difference in the patient reported measure of global H-RQOL and Life Satisfaction between the four groups despite the significant variation in the physical living and social life. The scores for global H-RQOL and Life satisfaction were similar i.e. >50%. Such an observation could result from the similar method of assessment of both these measures. Global H-RQOL and Life Satisfaction were measured on a single item although they have several aspects. Single item scales are not sensitive to the totality of the experience. Therefore, it is likely to miss out the true understanding of the impact of progression of foot complications on the different domains of global H-RQOL and Life Satisfaction. Similarly single item scales can fail to inform the precise picture of the patient's experience due to a disease and therefore make it difficult for the care providers to help them. The challenge of a single item scale to reflect the true picture of patient's experience regarding global H-RQOL and Life Satisfaction is analogous to i) confirming the diagnosis of a multi-system disease based on a solitary investigation or ii) studying the impact of a disease based on a single outcome measure in research environment or iii) trying to achieve comprehensive rehabilitation with a single therapeutic ntervention. Rather what is necessary is to profile H-RQOL to identify specific problem areas in this experience with the objective of planing appropriate therapy to give maximum benefit to the patients with diabetic foot complications.

Summary of H-RQOL:

With the progression of physical impairment from DMPN to DFU to PFA to TTA the physical aspect of H-RQOL showed a significant decline. Although social function varies significantly between the four groups, it is interesting to note that patients with healed PFA appear to demonstrate better social life compared to the patients with DFU although the difference is non-significant. Irrespective of the severity of physical impairment caused by diabetic neuropathy in terms of foot complications, all the patients demonstrated similar mental health status. Although their physical and social function differs, the 4 groups did not vary in their Vitality, their perception regarding General Health and Change in Health Status and neither do they experience any difference in Bodily Pain.

These findings may reflect the lack of rehabilitation care for diabetic patients with current foot ulceration. The need for providing them with support to adjust to the complications and the depression accompanying their poorer health state has already been identified (Price 2004). The increasing evidence to emphasise the holistic rehabilitation of these patients should result in implementation of multi-disclipinary management regimens. It is established that patients attending a specialist foot clinic and receiving orthotic interventions have significantly improved H-RQOL whereas those not attending the clinic demonstrated a decline (Tyrrell, Phillips & Price 1998). Such evidence is promising in terms of rehabilitation efforts for improving H-RQOL of diabetic neuropathic patients at consequent stages of foot complications. Based on the findings from the present study it is probable that measures to improve physical function may contribute to the improvement in the physical aspects of H-RQOL.

5.7: Summary with respect to hypothesis testing:

5.7A: Primary hypothesis:

The findings of the present study demonstrate that there was a significant difference in the functional outcome between the four groups i.e. DMPN, DFU, PFA and TTA. The four groups demonstrated an overall decline in the level of functional outcome with the progression of impairment resulting from consequent stages of foot complications in diabetic neuropathic people. All the three domains namely Mobility, Activity and H-RQOL demonstrated an overall deterioration from DMPN to DFU to PFA to TTA (refer to Figure 4.25). The risk of plantar tissue injury to the entire affected foot because of the commonly performed weight-bearing task of mobility (i.e. walking) increased from DMPN to DFU to PFA group.

However, the individual components of the domain of mobility presented with slight variations in the pattern of decline. The four groups demonstrated a steady, consistent decline in their performance of STS task and gait, whereas the trend in standing balance and social aspects of H-RQOL varied. The balance of the TTA group in standing appeared to be better than the patients with PFA and DFU. The PFA group appeared to demonstrate better Social Life compared to patients with DFU.

The deterioration in functional outcome resulting from a progression of physical impairment due to foot complications can explain the adaptations noticed during the tasks of mobility such as STS transfer and walking. All these results suggest that there is an increasing need for rehabilitation of diabetic neuropathic patients from the DMPN to DFU to PFA to TTA groups. Additionally it is observed that the PFA group warrants a well-defined rehabilitation program to improve their stability and maximise overall function. It is not sufficient to merely salvage the limb by performing PFA. Similarly, in the case of patients with DFU, it is not enough to only treat the ulcers and provide foot care but they need training to specifically improve their stability in standing and measures to improve their social aspect of H-RQOL.

5.7B: Secondary hypothesis:

This study investigated whether the two foot conditions i.e. DFU & PFA varied in the severity of their impact on the functional outcome of diabetic neuropathic patients.
The findings demonstrate that there was no significant difference in the overall function of the DFU and PFA groups (refer to Figure 4.26).

Comparison between PFA and TTA groups revealed that the two groups did not show a significant difference in the overall function except in the domain of activity performance wherein the TTA group presented with low average daily walking performance compared to the PFA group.

Additionally the TTA group demonstrated less net knee and hip joint moments on the affected limb with a compensatory rise in ankle and hip joint moments on the contra-lateral limb during STS and less knee moments on the affected limb during walking compared to the PFA group. However, the two amputee patient groups did not vary in their overall function despite the major difference in the level of amputation. The non-significant results in most domains of functional outcome despite the major difference in the level of amputation reflect the effect of the discrepancy in the rehabilitation care of the two groups of patients. It is reasonable to expect that a combination of no attempts for rehabilitation of the PFA group and six months of rehabilitation of the TTA group can cause non-significant results in the functional outcome of the patients. The results of the present study clearly indicate that the potential benefits of PFA in terms of better functional outcome compared to major LEA will not be evident unless a comprehensive rehabilitation programme is defined for patients with PFA.

5.8: Summary of exploratory analyses:

The findings from the exploratory analyses demonstrated that the different domains of the proposed model of functional outcome were associated with each other. Although the purpose of proposing such a multi-dimensional comprehensive model of functional outcome was to provide an in-depth analysis and identify specific problem areas in each domain of function it was recognised that the implementation of such a model may not be feasible in routine clinical practice. Therefore appropriate outcome measures representing the individual domains of function were selected for the exploratory analysis (refer to Chapter 3: Material and Methods) with the objective of choosing a single outcome measure to represent the respective domain of mobility instead of performing a battery of investigations. The proposed model of function included four different domains i.e. Impairment, Mobility, Level of activity and H-RQOL.

Although it might not be surprising to note that the strength of the lower limb muscles was directly associated with gait velocity, the positively significant correlation between the two outcome measures confirms the association between the domains of impairment and mobility.

A previous study (multiple regression technique) has demonstrated the significant association of lower limb muscle strength gain (knee flexors and extensors and ankle dorsiflexors and plantarflexors) with gain in gait speed (p=0.02) (Chandler et al. 1998). In the present study among the three lower limb muscle groups, it was noticed that the strength of the positive correlation decreased from the ankle plantar flexors (r=0.397) to knee extensors (r=0.354) to hip extensors (r=0.298). Although all the 3 muscle groups were weakly correlated with the gait velocity, the relatively stronger correlation with the ankle plantar flexors could be explained by the fact that the distal lower limb muscles tend to be more commonly affected than the involvement of proximal muscles due to diabetic neuropathy which is a rare presentation (Kelkar, Masood & Parry 2000).

Within the domain of mobility, the 3 tasks of mobility namely the speed of STS transfer, standing balance and gait velocity were related to each other. Direct association between the speed of STS transfer and balance in standing indicates that the slower the patient is in completing the STS transfer, the more the instability in standing (r=0.224). Standing balance was negatively associated with the gait velocity (r= -0.546) indicating that the more the instability in standing, the slower the speed of walking.

Furthermore the slower the transfer of STS, the slower the gait velocity (r= -0.294). Significant correlations between the three tasks of mobility certainly confirm the association between the 3 common tasks of mobility chosen for analysis of this domain of function. However, the little to moderate strength of the correlations between gait velocity, speed of STS transfer and standing balance does not allow the choice of gait velocity (or any single outcome measure) as a single measure to represent the domain of mobility. The three tasks of mobility seem to inform different aspects of the domain of mobility. A previous study has demonstrated gait velocity as a useful clinical measure of function based on the correlations between i) walking speed and muscle strength (hip flexors r=0.59, extensors r=0.76 and abductors r=0.56; knee flexors r=0.63 and extensors r=0.51 and ankle plantarflexors r=0.55 and dorsiflexors r=0.63), ii) walking speed and Physical Performance test (r=0.77), iii) walking speed and Functional Reach test (r=0.54) and iv) walking speed and Sickness Impact profile (r=0.47) in diabetic patients with trans-metatarsal amputations (Salsich & Mueller 1997). However, the results from the present study do not suggest gait velocity as the single most appropriate clinical measure to evaluate functional outcome in diabetic neuropathic patients at consequent stages of foot complications. Further studies with logistic multiple regression would be necessary to explore the choice of gait velocity as a solitary clinical measure of functional evaluation.

The significant correlation between gait velocity and average daily strides (r=0.463), average daily strides and physical aspect of H-RQOL (r=0.372) and the capacity and performance of walking (r= -0.346) confirms the association between the 3 domains namely mobility, level of activity and H-RQOL and explains how the various domains within the model are linked to each other. However, the low to moderate strength of the correlations between the 3 domains does not allow choosing a single domain to reflect the complete functional outcome of diabetic neuropathic patients with foot complications or predict the functional outcome of these patients in different domains based on the results of a single domain.

Therefore, to summarise the findings from the exploratory analysis it is confirmed that the various domains of the proposed model to evaluate function are associated with each other and it is clear how they are linked to each other. However, the strength of the correlations between the domains and within the domains does not allow choosing a single outcome measure to represent each domain but they inform exclusive aspects of each domain. Therefore, individual assessment of each of the outcome measures is necessary to inform the complete picture of functional outcome of the diabetic neuropathic patients with progressive foot complications. However, the implementation of such an indepth model of functional outcome is not recommended in routine clinical practice. Therefore, the findings from the present study should be used to identify the specific problem areas in these patients and define a rehabilitation program accordingly to maximise the functional outcome. Thereafter to be able to monitor the level of functional outcome over time, assessment of each domain of function can be conducted in a cyclic process to form a complete picture. From the battery of outcome measures used to evaluate function, the measures chosen for exploratory analyses can be used for clinical evaluation because of their simplicity and feasibility. These can be assessed in a cyclic manner to complete the functional evaluation. Nevertheless, the risk of plantar injury needs consistent regular assessment to prevent further complications in terms of plantar tissue injury.

5.9: Implications for clinical practice:

5.9A: Theoretical implications:

The decline in the overall function of the diabetic neuropathic patients in terms of mobility, walking activity and H-RQOL calls for an urgent need to develop a focussed rehabilitation programme for each of these patient groups, which presents with specific needs over and above the challenges of diabetic neuropathy alone. Current clinical practice suggests that the regimen of rehabilitation is clearly defined in patients with TTA as against those with DFU, PFA and DMPN alone.

In the case of patients with DMPN, the multi-disclipinary team approach to the management of diabetic foot complications has helped to provide prophylactic foot care to these patients (Edmonds, Foster & Sanders 2004). However, the necessary measures to improve postural stability, tasks of mobility and walking activity still need to be implemented in clinical practice.

Rehabilitation of patients with DFU in addition to wound management and foot care is still new to clinical practice. Current clinical practice shows that adequate emphasis on the care of the surviving foot is still in development and needs to be a part of routine foot care delivered to diabetic neuropathic patients with ulceration. It is now recognised that the management of patients with diabetic foot ulcers should not be confined to meticulous attention to footcare but must always include rigorous assessment of the patient's overall health (Walsh 1995).

Patients with PFA appear to be attended to only upto the point of healing of the amputation. Rehabilitation of the PFA patients following healing of the amputation wound tends to be confined to the referral of the patient to the department of surgical appliances for footwear.

The findings from the present study have highlighted the acute need for rehabilitation of the diabetic neuropathic patients with DFU and PFA in the various domains of function. They need substantial training to improve the performance of the daily tasks of mobility such as STS, balance in standing position, walking, adequate protection of the affected and the surviving foot during walking, cardio-respiratory capacity to perform activities of daily life and improve their H-RQOL.

Even in the case of TTA patients, there seem to be very few considerations made to provide the diabetic neuropathic amputee patients with specific care. It needs to be highlighted that all patients with TTA cannot be treated as a single entity irrespective of the cause of amputation. Diabetic neuropathic patients with TTA need special attention in terms of cardio-respiratory fitness and care of the surviving foot because of the low cardio-respiratory capacity and the increased risk of plantar injury shown in the study.

There is enough evidence to support the role of exercise in DM and plan/formulate guidelines for rehabilitation of these patients with DMPN. However, the following discussion on the role of exercise in DM will indicate that to date the investigation pertaining to the metabolic effects of various interventions of physical exercise in diabetic people have hardly considered the problems associated with DM such as diabetic neuropathy and its related foot disorders.

Although the following section includes a preface, which reviews the literature, describing the role of exercise in DM, this section is best suited here in the text followed by the clinical implications and suggestions to clinical practice.

5.9B: Role of exercise in DM:

Regular exercise has been recommended for diabetic patients for many years and was identified along with diet as one of the three components of good therapy by Eliot Joslin in the 1920s (Schneider & Ruderman 1986). However, there is very little known about the specific exercise program necessary for the diabetic population, which presents with specific needs at different stages of its complications.

Regular physical exercise has been known to be beneficial in the treatment of Type 2 DM (Schneider & Ruderman 1986, Sato 2000, Tudor-Locke, Bell, & Myers 2000, Maiorana et al. 2002, McCarty 2002, Swartz et al. 2003, Bhaskarabhatla & Birrer 2004, Ozdirenc, Kocak, & Guntekin 2004). It has been a measure for improving overall glucose control, especially in Type 2 patients and in the prevention of premature vascular disease (Schneider & Ruderman 1986). In well-controlled diabetic patients, physical exercise promotes utilization of blood glucose and lowers blood glucose levels. Whereas in poorly controlled diabetic patients with ketosis, physical exercise results in further rises in blood glucose, free fatty acids and ketone body concentrations (Sato 2000). Such an effect can be explained by the direct relationship between insulin sensitivity and aerobic fitness, measured by O_2 consumption indicating that the trained individual will have a greater insulin sensitivity and capacity to transport and utilise glucose in skeletal muscle (Kirwan et al. 2000).

Even a single bout of exercise has been shown to improve insulin sensitivity in Type 2 diabetic patients. As a result, glucose utilisation is greater and glucose production by the liver is decreased. This improvement is associated with an increase in the content of glut-4 mRNA and protein in skeletal muscle cells thereby facilitating the transport of glucose across the plasma membrane. Insulin sensitivity can be improved in obese and Type 2 diabetic patients, independent of weight loss. However, this effect is transient and lasts for approximately 24-72 hrs. Therefore, regular exercise is important for the long-term enhancement of insulin sensitivity (O'Gorman & Nolan 2005). Swartz et al. (2003) have recommended 10,000 steps/day for improved glucose tolerance in overweight women at risk for Type 2 DM (Swartz, Strath, Bassett, Moore, Redwine, Groer & Thompson 2003). Moreover a report based on literature review indicated that a low-fat, whole-food vegan diet, coupled with daily walking exercise, leads to rapid remission of neuropathic pain in the majority of Type 2 diabetic patients expressing this complication (McCarty 2002). It is believed that concurrent marked improvements in glycemic control presumably contribute to this benefit but are unlikely to be solely responsible. Consideration should be given to the possibility that improved blood rheology i.e.decreased blood viscosity and increased blood filterability plays a prominent role in mediating this effect (McCarty 2002).

It needs to be noted that in the rapidly developing focus on the role of regular physical exercise as an adjunct to diet and insulin in the management of Type 2 DM, very little consideration has been shown to the other potential problems that diabetic patients may be at risk for. Only one report was located expressing diabetic foot as a major concern in the implementation of exercise programme in this patient population (Schneider & Ruderman 1986). Both neuropathy and impaired circulation can pose challenges to implementing regular exercise in these patients.

In addition to the diabetic foot complications, the theoretical risk of accelerating degenerative joint changes suggest that high impact activities such as jogging should be discouraged (Schneider & Ruderman 1986) and alternative activities such as swimming and cycling should be used in patients with DMPN.

The findings of the present study complement the views of Schneider et al. (1986) and emphasise that diabetic patients with neuropathy related foot complications warrant a specific tailor-made exercise programme including non-weight bearing or partial weight-bearing aerobic exercise performed in appropriate foot-wear as an alternative to weight-bearing exercises such as walking and high impact activities such as jogging. In light of the findings from the present study, which indicate an increased risk of plantar injury to the patients with foot complications, it is recommended that regular inspection of the feet is mandatory in these patients.

Such reports and the findings from the present study reinforce the need for tailor-made monitored exercise programme for diabetic neuropathic patients at various stages of foot complications. Therefore, it is essential to consider the three dimensions of exercise prescription in the planning of the exercise regimen for this patient group namely the type, duration and intensity of exercise, ways of monitoring the exercise and adjunctive care during exercise e.g. protective footwear.

5.9C: Clinical implications and suggestions for further practice:

Role of Physiotherapy in the rehabilitation of four groups of patients with foot complications related to DMPN:

The findings of the present study clearly indicate the need for maximising the functional outcome of diabetic neuropathic patients at different stages of foot complications. By identifying the specific problem areas in the three domains of function, it has laid the groundwork for further research to investigate the effectiveness of suitable Physiotherapy interventions to improve functional outcome. Current clinical practice demonstrates very little evidence of the role of Physiotherapy in the rehabilitation of these patients. Although a review of literature reveals certain recommendations to clinical practice regarding the role of Physiotherapy in the management of diabetic foot complications such as gait modifications, joint mobility exercises and muscle strengthening, they appear to be very much at a stage of clinical recommendations rather than actual implementation in practice. This section outlines the potential role of Physiotherapy with the objective of maximising the functional outcome of the 4 patient groups in all the three domains namely: mobility; activity and H-RQOL.

5.9C (i): Mobility:

STS:

The findings of the present study reveal that the performance of the STS movement is asymmetrical in patients with DFU, PFA & TTA demonstrating marked asymmetry in the DFU and TTA groups. Although it is a convention to concentrate all the efforts of rehabilitation to correct the asymmetry of movement, these results suggest that the focus of training should be to facilitate the task, ensure the stability of the movement and safeguard the aging joints of the contra-lateral limb from the threat of increased joint reaction forces, which may consequently predispose them to further degenerative changes.

Options such as modifications in seat height (Burdett et al. 1985) and the use of arm rests (Seedhom and Terayama, 1976, Ellis et al. 1984) have been evaluated to decrease lower limb joint moments. There was a consensus that increasing the height of the chair seat and rising with the assistance of the arms decreased the forces in relation to the knee and to a lesser extent the hip joint (Kerr, White, Mollan & Baird 1991). Specially designed chair such as the E-Z Up Artherapedic Chair (seat height=0.64m with an adjustable foot rest which is swung out of the way when the person leaves the chair) can significantly decrease the joint moments needed at the hip and knee making the STS transfer less stressful to the joints (Burdett et al. 1985). In addition to the high seat, the ejector mechanism has proved effective for rising from a chair, as it does not necessitate the use of a footstool, a possible obstacle contributing to falls (Munro et al. 1998). However while selecting the appropriate chair for these patients with foot complications it is necessary to be cautious as specially designed chairs may be comfortable for the elderly but may not facilitate the act of rising (Wheeler et al. 1985).

Strengthening of the lower extremity muscle groups and training in terms of using appropriate chair height and armrests during rising are recommended to meet the training requirements.

To summarise, patients with DFU, PFA and TTA need to be trained to rise from a high seat with the help of the armrests in addition to wearing protective footwear during this common mobility task.

Standing balance: A steady decline in standing balance with consequent stages of foot complications demands greater emphasis and implementation of rehabilitation training to improve balance in all these patient groups with specific emphasis on patients with DFU and PFA wherein appropriate measures need to be defined and evaluated.

Researchers have already evaluated certain measures to improve balance in patients with peripheral neuropathy. The use of a cane has been demonstrated to reduce balance loss and improve postural stability in these patients (AshtonMiller et al. 1996, Dickstein, Shupert & Horak 2001). A brief specific exercise regimen has been shown to improve the clinical measures of balance in patients with peripheral neuropathy. The patients participating in the study performed the exercise interventions daily on a firm surface for 3 weeks (it is unclear whether they were supervised or un-supervised). The exercise regimen included: 1) warm up-open chain active ankle ROM exercises, 2) Bipedal toe raises and heel raises, 3) Bipedal inversion and eversion, 4) Unipedal toe raises and heel raises, 5) Unipedal inversion and eversion, 6) Wall slides and 7) Unipedal balance for time. It needs to be highlighted that most exercises in this regimen were weight-bearing exercises, which cannot be prescribed to patients with current ulceration. However, the results from this study demonstrate the beneficial role of active exercise regimen in patients with peripheral neuropathy.

However, appropriate modifications are required to structure a specific exercise programme for patients with DFU since the regular weight-bearing training to improve balance cannot be recommended in these patients. In the case of patients with DFU, non-weight bearing options such as goal-oriented active exercises of the foot can be thought to contribute towards the improvement of balance in the standing position. At this stage, the implications of active exercises on the haemodynamics of the ulcerated foot are not clear. However, they could be implemented safely on the contra-lateral foot. Further research is necessary to investigate the effectiveness of these therapeutic options in patients with DFU. In the meanwhile use of a cane/walking stick can be suggested in these patients to ensure postural stability.

It is clear from the results of the present study that the patients with PFA appear to be neglected in terms of balance training compared to patients with TTA in whom balance training is an integral part of the rehabilitation program (Broomhead 2003). A similar exercise program can be used to train the balance of the patients with PFA. Single and dual task form of weight-bearing exercises could be suggested to improve the balance of the patients with PFA. Mechanical balance training devices have also been used for balance training however; these devices have been used in patients with hemiparesis and trans-tibial amputations (Matjacic & Burger 2003, Matjacic et al. 2005). Further research is necessary to develop a balance-training program for these patients and test its effectiveness.

Even in the case of patients with TTA wherein balance training is already streamlined in clinical practice, it needs to be highlighted that the diabetic amputee patients require added attention because it is known that the standing balance of dysvascular amputee patients is inferior to that of traumatic amputee patients (Hermodsson, Ekdahl, Persson & Roxendal 1994). Therefore, it is recommended that the diabetic amputee patients should be given special consideration in the balance training programmes.

To summarise all 4 diabetic neuropathic patient groups need training to improve their standing balance and reduce the likely morbidity caused by falls. However, there is a lack of such training programmes for all these patient groups although there are certain measures defined to improve their balance. It needs to be noted that some of the therapeutic options suggested here have not been fully evaluated and therefore they should be considered as theoretical suggestions until they are proved to be effective.

Gait:

It is noted from the present study that gait assumes an increasingly conservative pattern with the progression of foot complications from neuropathy alone to TTA demonstrating a decline in gait velocity, cadence and stride length across the four groups. Additionally the

PFA group walked with less peak ankle plantar flexor moment on the affected limb compared to the DFU and the TTA group and the TTA group walked with less knee moment on the affected limb compared to the PFA group.

These findings may tempt rehabilitation therapists to increase the gait velocity of the patients with DMPN, DFU, PFA and TTA in an attempt to restore a near-normal gait pattern. Moreover, there is evidence to state that gait speed is a useful tool for objective monitoring of the progress of elderly patients undergoing rehabilitation (Potter et al. 1995). However, it needs to be emphasised that the conservative gait pattern is known to contribute to the stability of walking in diabetic neuropathic patients (Dingwell, Cusumano, Sternad & Cavanagh 2000) and therefore needs consideration to retain it with an intention of reducing the potential risk of falls. Deliberate instructions to continue to walk with such a gait pattern may emphasise the role of a conservative gait pattern in maintaining the stability of a dynamic posture.

Moreover, in the light of evidence, which states that plantar pressures are known to rise with increasing gait velocity, retaining the conservative gait pattern appears to be beneficial for the diabetic neuropathic patients. Additionally the use of a cane in providing further stability is recommended in patients with severe balance impairment. Furthermore, the direct association between the strength of the lower extremity muscles on the affected limb and gait velocity suggests that specifically tailored strengthening programme designed for the lower extremity muscles should help to improve the efficiency of gait in these patients.

Moreover strengthening of the ankle plantar flexors and appropriate modifications in the footwear of the patients with PFA may have a role in improving the push-off on the affected limb. Until the effect of ankle plantar flexor strengthening on the plantar ulcer is not evaluated training the patients with DFU to walk with a hip strategy may appear to be a useful strategy.

5.9C (ii): Plantar pressure distribution:

The findings of the present study demonstrate that plantar pressures over the affected foot increase with the progression of diabetic foot complications from neuropathy alone to PFA during walking. Additionally the contra-lateral foot is at a potential risk of plantar injury in these patients due to increased pressures. It is already established that the plantar stress (foot pressures) produced by walking is comparable to other daily ambulatory activities (Maluf, Morley, Richter, Klaesner & Mueller 2004). Therefore, it is emphasised that appropriate protection of the diabetic neuropathic foot on the affected and contra-lateral limb during all the daily ambulatory activities in addition to walking is mandatory to prevent further risk of injury in this patient group.

In the literature, various measures to reduce plantar pressures during walking have been suggested. Therapeutic footwear since long has been recognised as a measure to reduce plantar pressures in these patients. However, although there is a volume of literature identifying the suitable footwear for patients with neuropathy alone, with current plantar ulceration and partial foot amputation (Boulton et al. 1986, Gramuglia, Palmarozzo & Rzonca 1988, Mueller et al. 1989, Huband & Carr 1993, Perry et al. 1995, Ashry et al. 1997, Catanzariti et al. 1999, Bus, Ulbrecht & Cavanagh 2004), there is limited evidence to suggest the best appropriate footwear for prophylactic foot care in the presence of DMPN. Moreover, the stability during walking and the ease of walking with such shoes remains unexplored. Certain types of footwear are fore-foot weight-relieving whereas others are heel weight-relieving. Footwear primarily designed to reduce plantar pressures might not be appropriate in terms of stability. Considering the decreased stability and reduced daily walking activity in these patient groups, it is mandatory that the prescription of appropriate footwear needs to account for stability during walking and the ease of walking along with the primary objective of protection of the surviving foot during weight-bearing activities.

Moreover, the implications of such protective footwear on the contra-lateral foot need to be investigated as well to enable appropriate prescription of the footwear to this patient group, which is already at risk of plantar injury. Lavery et al. (1997) have confirmed that the contra-lateral pressures were not increased with the TCC use in patients with plantar ulceration. However, the implications of the remaining proposed footwear on the contra-lateral foot of the other diabetic neuropathic patient groups remain unexplored.
Researchers have investigated the role of specific gait patterns in the reduction of fore foot pressures. They have documented that a shuffling gait pattern can decrease the peak plantar pressures under the 1-2 MT (up to 57.8%) and the hallux (up to 63.2%). A hip pull-off pattern can decrease the peak plantar pressures at the fore-foot (up to 27 %) and a step-to walking pattern can decrease the peak pressures at the fore foot up to 53% (Brown & Mueller 1998, Kwon & Mueller 2001). There is also evidence to suggest that compared to using the normal (ankle) strategy, using the hip strategy showed a significant 27% decrease in forefoot and a 24% increase in heel peak plantar pressures (Mueller et al. 1994). However, it needs to be recognised that both these studies have evaluated the efficacy of the suggested gait patterns in diabetic neuropathic patients and non-diabetic controls. Therefore, they can be directly implemented safely in diabetic neuropathic patients alone. In the light of the gait alterations produced by partial foot amputations and TTA the

strategy of prescribing these gait patterns need to be revisited to investigate their effectiveness in these patient groups.

Finally yet importantly, the value of prophylactic foot care has already been identified in diabetic neuropathic patients to prevent plantar injury (Hunt 2002, Jeffcoate & van Houtum 2004). What needs emphasis is the prophylactic care of the contra-lateral foot in the diabetic neuropathic patients at consequent stages of foot complications, which are identified with risk of plantar injury in the present study. Moreover, there is emerging evidence to suggest that in diabetic unilateral amputee patients, foot screening and education programmes aimed at neuropathy alone are not sufficient to prevent contra-lateral amputation. Prophylactic foot care programs and strategies for diabetic unilateral amputees should therefore place greater emphasis on peripheral vascular assessment to identify patients at risk and likely to benefit from timely intervention (Carrington et al. 2001).

To summarise, in addition to the preliminary foot care delivered to the diabetic neuropathic patients it needs to be recognised that the specific patient groups at consequent stages of foot complications such as DFU, PFA and TTA present with specific needs. Therefore, it is necessary to highlight that they warrant tailor-made strategies to reduce the plantar pressures and thereby prevent the risk of injury.

5.9C (iii): Activity level:

Capacity:

It is clearly evident from the current study that physical capacity of diabetic patients decreases with the progression of foot complications indicating the need for tailor-made monitored exercise programmes for diabetic neuropathic patients at various stages of foot complications. Exercise measures to improve physical capacity should consider the three dimensions of exercise prescription in the planning of the exercise regimen for these patients namely the type, duration and intensity of exercise (McArdle, Katch & Katch 2001), ways of monitoring the exercise and adjunctive care during exercise e.g. protective footwear.

A recent study has demonstrated that a supervised in-patient physiotherapy programme is a safe and effective intervention in Type 2 diabetic patients, which reduces physical impairment and improves functional ability (Ozdirenc, Kocak & Guntekin 2004). In a randomised controlled trial, the researchers studied the effect of an exercise programme which included 5 minutes of warm up (breathing exercises, simple flexibility exercises of the trunk, upper and lower limbs), 10-30 minutes of cardiovascular exercise (walking in a corridor), posture exercises and strengthening exercises using therabands for training the lower limbs and 5 minutes cool-down exercise (breathing exercise and flexibility exercise). The exercise programme was designed to be of submaximal intensity performed 5 times a week, lasting 20-45 minutes for an average of 12 days. Although the authors have shown that the exercise program was effective in reducing the physical impairment and improving the functional limitation (measured on the basis of 6 min walk test and the patients perception of exercise intensity measured on Borg scale) of the diabetic patients; there is no mention of the neuropathy status of these patients and the implications of such a weight-bearing exercise program on diabetic neuropathy related foot complications.

Recently researchers have discussed the risk of plantar injury resulting from walking in addition to the benefits of walking for the diabetic neuropathic patients (Kanade et al.

2006). Therefore, non-weight bearing exercises such as swimming or partial weight-bearing exercises such as cycling with appropriate footwear may appear to be reasonable options for patients with DMPN, PFA and TTA. However, the plantar pressures during cycling need to be investigated in these patient groups before it can be recommended as an exercise option. Active foot ulceration poses challenges to the prescription of the type of exercise for these patients. Even swimming cannot be prescribed as an option for them for obvious practical reasons of hygiene and cross-contamination. Recently the value of physical exercise in the healing of acute and chronic wounds is also gaining recognition based on the growing body of pilot evidence. It is suggested that the healing benefits of exercise are related to an increase in cardiovascular or respiratory fitness and / or neuroendocrine responsiveness (Bolton 2006). However, the specific effects of physical exercise on diabetic foot wounds are unclear and need to be investigated before prescribing a particular exercise regime for these patients.

In the light of the multisystem involvement of DM, the extent of involvement of the other systems such as cardiac, respiratory and renal need to be considered in the prescription of the duration and type of exercise. However, it is evident that irrespective of the duration and intensity of the physical exercise, regular rest periods interspersed with physical activity are essential even during partial-weight bearing exercises such as cycling to avoid the cumulative plantar stress, which may have an underlying potential risk for plantar injury.

Literature has also documented that in addition to improving metabolic control, physical exercise training also improves various aspects of HRQOL in patients with DM. Besides the enhanced cardiorespiratory capacity, this is an important subjective benefit in patients with longstanding insulin dependent (Type 1) diabetes mellitus (Wiesinger et al. 2001).

Performance:

Although it is evident that walking activity decreases with progression of foot complications it is not automatically recommended to increase the level of walking activity since the safe threshold for the volume of walking is still unclear in this patient population. Based on the findings of the current study it can be suggested that diabetic patients with foot complications should continue to perform the essential volume of walking required for daily living though it is difficult at this stage to prescribe a safe limit of daily walking. On one hand it is possible that the patients walk too little and become prone to physical deconditioning since capacity and performance of walking are shown to be associated with each other in the present study, whereas on the other hand they can walk excessively and place the foot at an increased risk of injury. Therefore, it is clear that this area needs further exploration. However, patients can be informed that sudden changes in activity and the routine loading of plantar tissues can cause plantar injury although an absolute value of peak plantar pressure or step count responsible for plantar injury is not known (Lott, Maluf, Sinacore & Mueller 2005).

Additionally it is necessary to strongly emphasise the importance of protective footwear for the affected and the contra-lateral foot during walking.

5.9C (iv) H-RQOL:

The findings of the current study indicate that there is a need for improvement of the H-RQOL of diabetic patients with foot complications in the physical and social aspects. The need for providing support to patients with diabetic foot ulceration to adjust to the complications and the depression accompanying the poorer health state has already been identified (Price 2004). Moreover, it is established that patients attending a specialist foot clinic and receiving orthotic interventions have significantly improved H-RQOL whereas those not attending the clinic demonstrated a decline (Tyrrell, Phillips & Price 1998). Such evidence is encouraging for further investment in rehabilitation efforts aimed at improving H-RQOL of diabetic neuropathic patients with foot complications in addition to patients with diabetic foot ulceration.

Based on the findings from the present study, which demonstrate an association between the gait velocity and the average daily walking performance and the association between the average daily walking performance and the physical aspect of the H-RQOL; it is the conviction of the researcher that measures to improve the physical performance may contribute to the improvement in the physical aspects of H-RQOL. Whether an improvement in physical function will lead to better social and mental health is not known. Further research in this area should be able to address such questions.

To summarise, based on the findings from the present study it is evident that the need for rehabilitation of these patients increases with the progression of foot complications. It has been identified that Physiotherapy has a wide scope in this area of rehabilitation along with the expertise input from the remaning multi-disclipinary foot care team to maximise the functional outcome.

Conventionally the focus has always been on delivering optimal care only after an event of major LEA. Although rehabilitation care is defined for these patients, what needs more emphasis is that diabetic patients with amputations present with specific needs. The presence of peripheral neuropathy warrants foot care of the surviving foot and the multi-system nature of the disease demands measures to improve physical capacity concurrently.

5.10: Limitations to the study: Issues beyond the scope of the study

5.10A: Study design:

The limitation of this study lies in the choice of a cross-sectional design rather than a longitudinal study. The robustness of the study would increase with a longitudinal design to investigate the functional outcome with the progression of foot complications in the diabetic population. However considering the time scale required for a longitudinal study and the cost involved, the choice was to explore the research question with a cross-sectional design. However, this cross-sectional study design came with its challenges because of the difficulties to recruit an adequate number of patients with PFA. In terms of the sample size the PFA group had a low number of patients (n=16) compared to the estimated sample size (n=23). Recruitment of an adequate number of subjects with healed unilateral partial foot amputations was a challenge due to 3 major factors namely i) lower incidence of PFA compared to major LEA at our centres, ii) incidence of problems such as wound failure or early progression to higher levels of amputation or iii) presence of acute symptoms of neurological or musculo-skeletal disorders, which might have introduced a confounding bias in the interpretation of the results. However, a reasonable sample size of the PFA group allowed comparing the 4 groups statistically.

Findings from another study conducted at the University of Bristol (unpublished) support our experience of difficulties in recruiting patients with diabetic foot complications.

Ninety-seven patients with diabetic foot ulceration were recruited for the study. Out of these 16 (16.5%) patients dropped out for personal / unknown reasons. Of the remaining 81 patients, there were 4 (5%) amputations, 4 (5%) deaths, and 5 (5.2%) withdrawals through illness over a period of 24 weeks of the study. This was a longitudinal study as against the present cross-sectional study. Therefore, the intention was not to compare the two studies but merely to share the difficulties encountered in recruiting diabetic neuropathic patients with healed unilateral PFA.

The present study may also be criticised for not including a matched group of non-diabetic healthy subjects for comparison with the diabetic neuropathic patient groups. Although it would be an ideal proposal the inclusion of such a group would make the study bigger and the bigger study would be faced by its challenges e.g. more number of patients, increased time and expenses. Moreover, it was not mandatory to include a healthy group, as most of the normative data already existed in the literature. Therefore, findings from such a group would not add to the existing body of knowledge. Furthermore, the focus of the present study was to investigate the functional outcome in diabetic neuropathic patients following subsequent foot complications.

5.10B: Patient groups:

The aim was to recruit a homogenous group of patients in terms of location of plantar ulceration and level of foot amputations. The different sites of plantar ulceration in the DFU group and the different levels of foot amputation in the PFA group posed limitations on the interpretation of results of the biomechanical variables. The maximally affected variables were those related to gait especially plantar pressure distribution. Results from a homogenous group would result in a specific picture of gait pattern and pressure over specific plantar areas. Therefore, in the light of the heterogeneous nature of the two groups, the variable of total peak pressure over the entire foot was relied on more than the specific plantar areas in the interpretation of the results.

However, it needs to be highlighted that homogenous groups in terms of amputation level and site of plantar ulceration would be less representative of the general diabetic patient population with foot complications.

5.10C: Data collection:

Measurement of plantar pressure distribution on the affected and the contra-lateral foot during STS, standing and walking would have allowed a precise comparison of the relative plantar load bearing between the 3 weight-bearing tasks. Although evidence from previous studies and the present study can be assimilated to indicate that pressures increase from standing to walking, comparison between the 3 common weight-bearing mobility tasks can reveal whether there is a variation in the specific plantar areas predisposed to higher plantar pressures during these common tasks of daily life.

Additionally, standardised evaluation of foot deformities would also contribute towards identification of specific plantar areas predisposed to higher pressures during these weight-bearing tasks of ADL. The present study adopted a reasonably practical approach of identifying the alteration in the medial longitudinal arch to rule out the possibility of variation in the proportion of forefoot to hindfoot pressure distribution due to obliteration of the medial longitudinal arch of the foot.

5.10D: Statistical analysis:

Involvement of large number of variables to address the research question of the present study introduced threats of multiple testing during comparison of the 4 groups. A dilemma existed between the possibility of conducting novel investigations in a minimally explored area of interest (e.g. specific performance of patient groups with DFU, PFA and TTA) using multiple testing on one hand whereas on the other hand there was a danger of data dredging. Although the option of conducting several satellite studies with the objective of assimilating the information to address such a research question is tempting, it is challenged by the lack of consistency / homogeneity in the study sample. Such a problem brings the discussion back to the ideal proposal of a longitudinal study.

Secondly, considering the large number of variables it was not possible to estimate the power of the study to be able to detect the significant degree of change in all the variables. Since the focus of the present study was largely based on kinesiological variables of function, the sample size was inadequate to investigate all the H-RQOL measures. Therefore, the interpretations from the findings from the H-RQOL measures were limited by the comparative sensitivity of the measurement tool.

5.11: Recommendations for future research:

Review of the literature has clearly indicated that the area of evaluation of functional outcome in diabetic neuropathic patients has been minimally explored so far. The present study has performed the groundwork necessary for further investigation. It has made a remarkable addition to the existing body of knowledge by identifying the specific problem areas in each of the three domains of function of diabetic neuropathic people at consequent stages of foot complications i.e. common tasks of mobility, level of walking activity and its implications on plantar weight-bearing and the H-RQOL. In this process of investigation, it has opened the doors to several research questions, which need further investigation to be able to inform clinical practice and develop specific rehabilitation regimen for the diabetic neuropathic patients, who present with specific challenges at different stages of foot complications.

Although there has been discussion of the role of therapeutic interventions in the improvement of joint range of motion and muscle power in patients with foot complications related to diabetic neuropathy (Mueller, Salsich & Strube 1997, Salsich & Mueller 1997, Goldsmith, Lidtke & Shott 2002), the findings from the present study have identified the potential role of Physiotherapy in the improvement of various domains of function in these patients.

Additionally it would be interesting to study the association between the course of progression of neuropathy and diabetic foot complications in a longitudinal study.

There are volumes of literature available to discuss the role of various dressings in the healing of diabetic foot ulcers. However, the effect of these wound dressings on standing balance is an equally important consideration in case of a diabetic neuropathic patient with impaired sensory feedback from the feet. Further research is essential to study the effectiveness of various therapeutic interventions to improve standing balance in diabetic neuropathic patients at the stage of active ulceration, partial foot amputations and TTA in light of the findings of the present study, which have demonstrated a decline in the standing balance with progression of foot complications.

Previous studies have suggested certain gait patterns to minimise the peak plantar pressures for diabetic neuropathic patients (Mueller et al. 1994, Brown & Mueller 1998, Kwon & Mueller 2001, Drerup et al. 2004). Considering the specific needs of patients with DFU, PFA and TTA, it is necessary to explore interventions in gait specific to the needs of these patient groups. Taking into account the increased energy expenditure and the decreased daily walking it is necessary that proposed gait modifications be of reasonable merit in terms of maintenance of balance and metabolic gait efficiency whilst foot protection is ensured to be adequate.

Moreover, it would be interesting to explore the association between capacity and performance of daily walking and whether daily walking influences social function of people with diabetic foot complications. The precise understanding of the cause-effect relationship between capacity and performance of daily walking warrants investigation. However, irrespective of the nature of the relationship between the two factors, the need for improvement of physical capacity of patients is evident from the present study. Further research is necessary to arrive at a specifically tailored aerobic exercise program with equal emphasis on foot care and physical fitness for this patient population, which presents with specific challenges at different stages of foot complications.

Additionally the correlation between daily walking performance and self-reported measure of mobility and physical aspect of H-RQOL would be of interest to identify the effect of foot complications on patient's own perception of mobility and H-RQOL. Moreover, H-RQOL needs to be further investigated in these patient groups by deciding the power of the study based on the H-RQOL measures to detect a difference of 10 point on the scale. Based on the findings from the association between the domains of mobility, walking activity and physical aspect of H-RQOL in the present study, it may be true that measures to improve physical function may contribute to improvement in physical aspects of H-RQOL. Assessment of H-RQOL before and after intervention by means of a rehabilitation program is necessary to confirm this idea.

Chapter 6: Conclusion

Based on the results of the present study the primary null hypothesis that there is no difference in the functional outcome in diabetic patients at consequent stages of diabetic foot complications was rejected. It was inferred that there is a significant difference in the functional outcome in diabetic patients at consequent stages of foot complications. There was an overall decline in all the three domains of function namely the mobility tasks i.e. STS, standing balance and gait; the capacity and performance of activity i.e. walking and the H-RQOL especially the physical aspects of H-RQOL with the progression of physical impairment related to diabetic neuropathy from DMPN to TTA group. The increasing risk of plantar injury from DMPN to DFU to PFA group on the affected foot during an essential common weight-bearing task such as walking warrants a greater and precise focus on walking strategy, prophylactic foot care and footwear, which is appropriate in terms of providing adequate protection to the foot, stability during walking and facilitate necessary level of walking activity.

Although there was evidence to suspect that diabetic patients with healed partial foot amputations may perform better than patients with active foot ulceration the results demonstrated that there was no significant difference in the functional outcome between these two groups. Further investigation with a larger sample size in both groups is recommended to confirm the findings from the present study.

There was no significant difference in the functional outcome of diabetic neuropathic patients with minor amputations e.g. partial foot amputations and major amputations e.g. trans-tibial amputations except that the patients with TTA walked significantly less compared to the patients with PFA. The similar performance of the TTA group compared to the PFA group despite undergoing a major amputation may be attributed to successful implementation of defined rehabilitation care of the patients with major amputations such as TTA and lack of rehabilitation measures planned for diabetic neuropathic patients following PFA.

There is a need for implementation of therapeutic measures to maximise functional outcome of diabetic patient groups with neuropathy alone, foot ulceration and partial foot amputations, which currently appear to be neglected. It is evident that additional efforts are essential to further maximise the functional outcome of patients with TTA. Moreover, the multi-system involvement of DM warrants that the diabetic neuropathic patients with TTA need to be treated as a patient group with specific needs in terms of balance training, footcare during weight-bearing activities, aerobic capacity and support measures to improve the H-RQOL as against patients with amputations resulting from trauma or peripheral vascular disease.

The present study has made a remarkable addition to the existing body of knowledge by identifying the specific problem areas in each of the three domains of function of diabetic neuropathic people at consequent stages of foot complications i.e. common tasks of mobility, level of walking activity and its implications on plantar weight-bearing and the H-RQOL. It has also confirmed the association between the domains of the model proposed for functional evaluation namely mobility, level of activity and H-RQOL. However the strength of the associations do not allow identifying a single simple outcome measure for respective domain for the purpose of clinical assessment of function since the various outcome measures appear to reflect exclusive aspects of functional outcome.

However, the simple appropriate outcome measures chosen for exploratory analysis can be used to monitor the level of function of these patients in clinical practice.

Concurrently the in-depth information gathered from the present study can serve as an invaluable basis for the planning of a rehabilitation program for these patient groups. However further research is necessary to investigate the effectiveness of suitable Physiotherapy interventions and define a specifically tailormade multi-disciplinary rehabilitation programme for these patient groups presenting with specific challenges at different stages of foot complications with the objective of maximising functional outcome.

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Appendix 1

- Ethical approval: South East Wales Local Research Ethics Committees
- Ethical approval: Research and Development, Cardiff and Vale NHS Trust
- Ethical approval: Research and Development, Morriston Hospital, Swansea
- Invitation letter to the patient
- Information sheet to the patient
- Initial contact form
- Patient consent form
- Assessment sheet

Canolfan Gwasanaethau Busnes
Business Services Centre

South East Wales Local Research Ethics Committees
Direct Line: (02920) 402309/402420

Our ref: AD/JS/jl/03/5115

Dr R W M van Deursen
Senior Lecturer
Head of Physiotherapy Research & Postgraduate Studies
School of Health Care Studies
University of Wales College of Medicine
Heath Park
Cardiff

19 May 2004

Dear Dr Deursen

Re: 03/5115 - Foot and lower limb function and Quality of Life in people with diabetic neuropathy at four consequent stages of foot complications

Amendment number: **1**
Amendment date: **5/5/04**

The South East Wales Research Ethics Committee – Executive Sub Committee - PANEL B reviewed the above amendment at their meeting held on 19 May 2004.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

With regard to extending your research to additional sites. The new standard operating procedures for Research Ethics Committees in the UK state that where, following the issue of a favourable ethical opinion the chief investigator wishes to extend a single site study to additional sites with principal investigators, the chief investigator should submit an application for site specific assessment to their local Research Ethics Committee. A copy of Part C of the National REC form together with the local investigator CV should be provided to your local LREC. Please note that all documentation is available on the COREC website.

Cont/d...

Canolfan Gwasanaethau Busnes
Ty Churchill
17 Ffordd Churchill
Caerdydd, CF10 2TW
Ffôn: 029 20 402402 WHTN: 1809
Ffacs: 029 20 402403
DX 121720, Caerdydd 9

Business Services Centre
Churchill House
17 Churchill Way
Cardiff, CF10 2TW
Telephone: 029 20 402402 WHTN: 1809
Fax: 029 20 402403
DX 121720, Cardiff 9

NHS WALES GIG CYMRU

Approved documents

The documents reviewed and approved at the meeting were:

- **Notice of Substantial Amendment Form signed and dated 5 May 2004**

Membership of the Committee

The members of the Ethics Committee who were present at the meeting were Mrs A. Dowden (Chairman) and Dr I Doull (Consultant Paediatrician).

Management approval

Before implementing the amendment, you should check with the host organisation whether it affects their approval of the research.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

REC reference number:	**03/5115**	**Please quote this number on all correspondence**

Yours sincerely

A. Dowden.

Mrs A Dowden
Chairman, Panel B
South East Wales Local Research Ethics Committee
(Dictated but not signed)

NHS WALES GIG CYMRU

Cardiff and Vale NHS Trust Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

ƒf/Your ref
/Our ref
Health Telephone Network 1872
line/Llinell uniongyrchol

Heath Park, Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan, Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Tel: 029 20743742
Fax: 029 20745311
E-mail:Judith.Harris@cardiffandvale.wales.nhs.uk

From: Jane Jones
Trust R&D Manager
Radnor House

29 September 2004

Dr Robert Van Deursen
Department Of Physiotherapy
School of Health Care Studies, UWCM

Dear Dr Van Deursen

Project ID : 03/clc/1869 : Foot and lower limb function, mobility and quality of life of people with diabetic neuropathy at four consequent stages of foot complications.

The Trust R&D Office has received and reviewed the protocol amendments to the above project. There are no objections to the amendments, and the Trust R&D Office is happy for the project to continue. Please forward a copy of this letter to the ethics committee.

May I take this opportunity to wish you success with the project and remind you that as local lead investigator you are required to:

a) inform the Trust R & D Office if any external funding is awarded for this project in the future
b) maintain a record of the number of patients /samples in this study
c) complete any questionnaires sent to you by the Trust R & D Office regarding this project
d) comply fully with the Research Governance Framework[1], and co-operate with any audit inspection of the project files
e) undertake the project in accordance with ICH-GCP[2] and the Trust's Guidelines on Good Research Practice[3]
f) adhere to the protocol as approved by the Local Research Ethics Committee
g) ensure that your research complies with the Data Protection Act 1998

Yours sincerely,

pp. D. Cook

Dr Jane Jones
Trust R&D Manager

H:\My Documents\Investigator Correspondence\03-CLC-1869 Amendappr.doc

[1]www.word.wales.gov.uk/content/governance/governance-framework-e.pdf

[2]www.ich.org.html *
www.mrc.ac.uk/pdf-ctg.pdf
www.doh.gov.uk/research/documents/gcpguide.pdf

[3]www.uhw-web1/research/rd.html
www.wellcome.ac.uk/goodpractice

*A concise copy of the latest ICH-GCP Guidelines is available from the R&D office.
E-mail: Research.Development@CardiffandVale.wales.nhs.uk

Research & Development Consortium NHS

Please reply to:

R&D Consortium Support Office
Swansea NHS Trust
Morriston Hospital
SWANSEA
SA6 6NL

Telephone: 01792 704056
Fax: 01792 703910
E-mail: jemma.hughes@swansea-tr.wales.nhs.uk

16 May 2005

Dr Robert Van Deursen,
Director, Physiotherapy
Research & Postgraduate Studies
School of Health Care Studies
Cardiff University
Heath Park, Cardiff
CF14 4XN

Dear Dr Van Deursen,

ID: S04PAMS333 Foot and lower limb function and Quality of Life in people with diabetic neuropathy at four consequent stages of foot complications

The above project is registered on our database as an active project.

I would appreciate it if you would give me an update on the project's progress, including confirmation of the start date, projected end date, whether the project is on schedule and on budget.

Thank you for your co-operation in this matter.

Yours sincerely

Jemma Hughes
Research & Development Manager

Coleg Meddygaeth Prifysgol Cymru
University of Wales College of Medicine

Yr Uned Ymchwil Gwella Clwyfau
Wound Healing Research Unit

Date:

***CONTACT INFORMATION*:**
Tel: (029) 20744587 **Time:** 9.00am-4.30 pm
Email: KANADER@Cardiff.ac.uk

Dear

Re: Foot / Lower Limb Function in Diabetic Neuropathy.

The Department of Physiotherapy Education is conducting a study to investigate the 'Foot / Lower Limb Function in Diabetic Neuropathy' in collaboration with the Wound Healing Research Unit (WHRU), University of Wales College of Medicine (UWCM) and the Artificial Limb & Appliance Service, Rookwood Hospital.

The study is approved by the South East Wales Local Research Ethics Committee. The WHRU is supportive of the study and therefore those patients attending the Diabetic foot Clinics are contacted to know whether they would kindly consider participating in this study.

Please find an information sheet enclosed. **Should you need any further information about this study or are willing to participate in the study, please contact – Rajani V Kanade or Michelle Evans at the address mentioned above** or we will contact you in two weeks time to find out if you are interested in taking part.

Thank you for your kind attention.

Yours sincerely,

Prof. Keith Harding, Clinical Directorate, WHRU
Prof. Patricia Price, Director, WHRU, UWCM
Rajani V Kanade, PhD student, Physiotherapy
Michelle Evans, Research Technician
Dr. Robert van Deursen, Head of Physiotherapy Research, UWCM
Research Centre for Clinical Kinaesiology, Department of Physiotherapy Education
Ty Dewi Sant, School of Healthcare Studies
University of Wales College of Medicine, Heath Park, Cardiff

Enc

Please send correspondence to:
Wound Healing Research Unit, University of Wales College of Medicine, Cardiff Medicentre, Heath Park, Cardiff CF14 4UJ. Tel: +44 (0)29 2075 7744. Fax: +44 (0)29 2075 4217.
Yr Uned Ymchwil Gwella Clwyfau, Coleg Meddygaeth Prifysgol Cymru, Medicentre Caerdydd, Y Mynydd Bychan, Caerdydd CF14 4UJ. Ffôn: +44 (0)29 2075 7744. Ffacs: +44 (0)29 2075 4217.
Website: http://www.whru.co.uk

Coleg Meddygaeth Prifysgol Cymru
University of Wales College of Medicine

Adran Addysg Ffisiotherapi / Department of Physiotherapy Education

Cyfarwyddwr Addysg Ffisiotherapi
Director of Physiotherapy Education
Professor N. P. Palastanga, MA, BA, FCSP, DMS, Dip. TP, ILTM
Pro Vice-Chancellor
Director of Department
e-bost / e-mail: physiotherapy@cardiff.ac.uk

INFORMATION SHEET

Foot and lower limb function, mobility & quality of life of people with diabetic neuropathy at four consequent stages of foot complications.

What is the purpose of the study?
Diabetes mellitus is known to affect the foot causing impaired sensations and reduced blood flow to the foot leading to ulcers. These ulcers are notorious for healing and if infected might affect the underlying bone leading to the removal of the affected part of the foot in order to save the remaining limb. Despite the common occurrence of foot complications in these patients, there's little scientific evidence addressing the issue of their level of activity and quality of life (QOL) following various treatment options. Therefore, this study is aimed at investigating the function of the foot, the ability of these people to perform their activities of daily living and their QOL. The objective is to identify how Physiotherapy can help to improve the outcome of treatment.

Why have I been chosen?
Subjects with diabetes mellitus diagnosed as cases with sensory neuropathy are included in this study and therefore you are chosen. 92 subjects will be included.

Who is organizing the study?
The study is organized and funded by the Research Centre for Clinical Kinesiology School of Health Care Studies in collaboration with Wound Healing Research Unit, University of Wales College of Medicine, Cardiff. The total duration of the study is 3 years.

What will happen to me if I take part?
You would be required to visit the Research Centre for Clinical Kinesiology (RCCK), UWCM, Heath Park, Cardiff and the necessary measurements will be completed in a single visit to the RCCK. The measurement session would continue for approximately one and half hours. In case you have not monitored your blood glucose level the same morning, we would measure it with Medisense-Precision Q-I-D Blood Glucose Sensor. The investigator is trained specifically for the procedure and it is a minimally invasive technique, which most patients perform independently at home for regular blood glucose monitoring. You are not required to starve for the assessment but are expected to avoid consumption of alcohol in the previous 24 hrs as this might affect your balance during the measurements. Please read here below the sequence of the tests to be carried out. You are expected to follow the verbal instructions while performing the tests and would be allowed to rest in between the tests if required.

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School of Healthcare Studies, Tŷ Dewi Sant, Heath Park, Cardiff CF14 4XN
Ffôn / Tel. (029) 2074 2267 Ffacs / Fax: (029) 2074 2267

***Sequence of measurements*:**

- In case you have not measured the blood glucose levels the same morning we might need to do measure it with the blood glucose sensor which the patients generally use for self monitoring.
- The various tests include measurements of force, pressure, balance and energy expenditure during standing and walking.
- Range of movement at the hip, knee and ankle joints will be measured.
- The measurements will be followed by questionnaires: one of which is a mobility index and the other two are Health related quality of life questionnaires.
- Towards the end of the assessment session a Step watch will be strapped along the outer border of the right ankle joint, which needs to be kept on; *except while having a bath* for a period of one week.
- We request you to arrange to return the step watch activity monitor after a week to the RCCK and to expect a simple questionnaire after a period of 3 months to collect your feedback on the status of the foot / leg function then.

What is the device?
Digital video camera will be used to record the movement occurring at various joints of the lower limbs during the activities measured. Pressures on the sole of the foot during walking will be measured using an in shoe pressure system connected to a portable equipment anchored around the waist. A force platform will be used to assess the force exerted on the leg during walking and the balance during standing will be assessed. A heart rate monitor will be strapped to the chest wall which will monitor heart rate continuously during walking. Step watch activity monitor would record the level of activity.

Are there any disadvantages in taking part in this study?
There exist no reported side effects of any of these measurement procedures. **In case of concern please feel free to contact us at RCCK on the telephone number: 02920744587.**

What are the possible risks of taking part?
Tight strapping of step watch activity monitor might expose the subject to a low risk of developing edema around the ankle and foot in case of already compromised circulatory system due to vascular disease or increasing the volume of edema already present around the ankle and foot prior to the application of the step watch activity monitor. Correct strapping of the device is not known to be risky.
The subjects will be demonstrated the correct application of the device and will be instructed to inspect the ankle and foot regularly; remove the device immediately should they notice any such adverse effect and report to RCCK for further advice.

What are the possible benefits of taking part?
The information we derive from this study will help us to plan better treatment in the future for patients with diabetes mellitus developing foot complications and identify how Physiotherapy can help to improve the outcome of treatment.

Are there any restrictions on what I might eat or do?
The subject is expected to avoid consumption of alcohol 24 hours prior to participation in the study.

What if something goes wrong?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of the study, the normal National Health Service complaint mechanisms may be available to you.

Confidentiality – who will know I am taking part in the study?
Your medical records may be inspected by the Research Centre for Clinical Kinesiology for purposes of analyzing the results. All information collected during the course of the research will be kept strictly confidential. Any information leaving the Research centre will be anonymised so that you cannot be identified.

GP Notification:
Your GP will be notified about your participation in the study (on the behalf of the Wound Healing Research Unit, Medicentre, UWCM and Artificial Limb and Appliance Service, Rookwood Hospital).

L.R.E.C. Approval:
South East Wales Local Research Ethics Committee has approved this study.

What will happen to the results of the study?
The results of this study will be informed to you through postal services.

Contact for further information.
Should you need further information, please feel free to contact:
Ms. Rajani V Kanade / Ms. Michelle Evans
Tel: 02920 744587.
Research Centre for Clinical Kinesiology
Department of Physiotherapy Studies
School of Health Care Studies
University of Wales College of Medicine
Heath Park
Cardiff CF 14 4XN

This study is conducted at the Research Centre for Clinical Kinaesiology in collaboration with the Wound Healing Research Unit, UWCM, Cardiff under the supervision of Dr. Robert van Deursen, Senior Lecturer, Head of Physiotherapy Research, RCCK, School of Health Care Studies and Prof. Patricia Price, Director & Prof. Keith Harding, Head of the department of Surgery & Professor of Rehabilitation Medicine, Wound Healing Research Unit, Cardiff Medicentre, Cardiff CF 14 4UJ
Thank you for participating in this study. We appreciate your willingness to foster research activities.

Version date and number:
Version No: 2
Date: 3rd July 2003

Initial Contact Form

FOOT / LOWER LIMB FUNCTION IN DIABETIC NEUROPATHY- 2003

<u>Date of call:</u>..........................   <u>Time of call:</u> ....
Repeat call details (where necessary):
Explain why you are ringing
Remind about information letter from us – check they have received it
Are they interested in <u>possibly</u> taking part?   YES: (   )   NO: (   )
Have they got a few minutes to answer some questions now? Do they have any questions?
<u>If not</u> – most convenient day/time to ring back..

me...
dress...
....
....
. No.....................................

D.O.B..................
Age.....................
Male   (   )
Female (   )
Shoe size..........cm

gnosis: Diabetes Mellitus- NIDDM: (   ) IDDM: (   )
te of onset........./......../..........
cruitment Centre:
nsultant:
erapy:
....
....
....

vel of Amputation:...
ilateral: (   )   Bilateral: (   )
te of Surgery...

ot ulcers:
y past history of ulcers?   YES: (   )   NO: (   )
e:...
set:...
ilateral: (   )   Bilateral: (   )

Are you on any Medications:
YES: (   )   NO: (   )
<u>If yes</u> specify................................
....
....

Have you had any medical treatment or injuries to the lower limbs over the last 2 years?
<u>If yes</u> specify...................................
....

Any history of major heart, lung, orthopaedic, neurological or renal problems <u>If yes,</u> specify whether or not on renal dialysis...............................
....

Do you have optimal vision to be able to perform your daily activities?
YES: (   )   NO: (   )

Can you perceive the sensations over the foot as good as you can feel them on the face or the trunk?
YES: (   )   NO: (   )

Do you monitor your blood glucose levels by yourself at home?
YES: (   )   NO: (   )

Any causes of restricted walking?
<u>If yes,</u> specify.................................
....
....

Are you working? YES: (   )   NO: (   )

Preferred attendance time: .... am / pm / eve / any

Transport required: YES: (   )   NO: (   )

Requires parking ticket: YES: (   )   NO: (   )

Needing assistance to get to research centre: YES: (   ) NO: (   )

Do you need a wheelchair for transfer from your car? YES: (   )   NO: (   )

Any other requirements? YES: (   )   NO: (   )

Are you able to walk across a distance of at least 5 metres without help from others? YES: (   ) NO: (   )
Are you able to walk across a distance of at least 20 metres without help from others? YES: (   )NO:(   )

Any walking aids: YES: (   )   NO: (   )

<u>If yes:</u> specify indoors or outdoors..

Use of wheelchair: YES: (   )   NO: (   )

<u>If yes:</u> specify indoors or outdoors..

Requirements

Explain that there is need for subject to bring t-shirt and shorts. This is necessary, as the testing procedure requires a good camera view of the legs while they are moving. Changing facilities and toilet are available in the laboratory.

Final Checklist

Confirmation letter sent confirming date, time, location, duration and requirements.

Map of UWCM sent with both Ty Dewi Sant and the Research Centre for Clinical Kinaesiology (RCCK) highlighted.

Reminder call to be made day before the subject is to attend:

Date of call:.............................   Time of call:.......................... ....

Coleg Meddygaeth Prifysgol Cymru
University of Wales College of Medicine

Adran Addysg Ffisiotherapi / Department of Physiotherapy Education

Cyfarwyddwr Addysg Ffisiotherapi
Director of Physiotherapy Education
Professor N. P. Palastanga, MA, BA, FCSP, DMS, Dip. TP, ILTM
Pro Vice-Chancellor
Director of Department
e-bost / e-mail: physiotherapy@cardiff.ac.uk

Patient Consent Form

Study title: Foot and lower limb function, mobility and quality of life in people with diabetic neuropathy at four consequent stages of foot complications.

The patient should complete the whole of this sheet himself/herself **(Please circle one)**

1. Have you read **and understood** the patient information sheet, Version No: 1 Date: 19th May 2003 (Please take a copy home with you to keep) **YES/NO**

2. Have you had an opportunity to discuss this study and ask any questions? **YES/NO**

3. Have you had satisfactory answers to all of your questions? **YES/NO**

4. Have you received enough information about the study? **YES/NO**

5. Who has given you an explanation about the study?

   Dr/Mr/Ms ....

6. Sections of your medical notes relating to your participation in the study may be inspected by responsible individuals from (company name) or from regulatory authorities. All personal details will be treated as **STRICTLY CONFIDENTIAL.**

   Do you give your permission for these individuals to have access to your records? **YES/NO**

7. Do you understand that you are free to withdraw from the study:
   - At any time?
   - Without having to give a reason?
   - Without affecting your future medical care?
   - That details of your participation up to the time of withdrawal will be stored anonymously on file and may be used in the final analysis of data **YES/NO**

8. Has the doctor discussed circumstances when compensation may be due? **YES/NO**

9. Have you had sufficient time to come to your decision? **YES/NO**

10. Do you agree to participate in this study? **YES/NO**

11. Do you agree to your GP being advised of your participation in this study? **YES/NO**

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12. Do you agree to your findings from this research to be stored or disposed as necessary or to publish information for educational purposes with the provision that your name will not be associated with any of the results. This includes any visual record during the performance of the functional tasks, providing that the content is anonymized. **YES/NO**

PATIENT

Signed ....
Date ....
Name (BLOCK LETTERS) ....

INVESTIGATOR

Signed ....
Date ....
Name (BLOCK LETTERS) ....

WITNESS

Signed ....
Date ....
Name (BLOCK LETTERS) ....

I have explained the study to the above patient and he/she has indicated his/her willingness to take part.

Version date and number:
Version No: 1
Date: 19th May 2003

Research Centre for Clinical Kinesiology

Foot / lower limb function in Diabetic Neuropathy

ASSESSMENT PROTOCOL-2003

t ID: **Patient group:** A B C D **Recruitment centre:**

Age: yrs **Sex:** M F

ance: R L **Occupation:**

: cm inches **Weight:** kg

ı smoke? Yes No **Do you drink alcohol?** Yes No

ı live- alone With family With carer

ı sense a feeling of loss of balance? Never Rarely Usually

o you walk? Without walking aid With walking aid:

of DM: **NIDDM** **IDDM**

of loss of sensations:

'es No IHD: Yes No

atory / Any other cardiac disorders:

lo-skeletal disorders:

uropathic #: Yes / No **Neurological problems:**

ed any PT Rx for the foot complications due to DM? Yes / No

of amputation: **Date of surgery:**

ı experience any of the following sensations?

pain: Yes No *Phantom limb*: Yes No *Phantom pain*: Yes No

o ulcers: site: Onset time: Period of healing:

py for ulcer Mx: **Foot offloading advised: Complete / Partial / None**

ding device:

Brachial Index: mmHg

glucose level: mmol/l **Vision:** 3/

pressure: Supine: mmHg Standing: mmHg

Sensations: S-W monofilaments:

S-W MF's	Great toe		Ist MT Head		Vth MT Head		Heel	
	R	L	R	L	R	L	R	L
4.31								
4.56								
5.07								
6.65								

L R

Score: L___ R___ Total ____

Joint position sense	**1st MT-P**	**Ankle**	**Knee**
Right			
Left			

Vibration: 128 Hz	**Head of 1st MT**	**Med Mall**	**Tibial spine**	**Tibial tubercle**
Right				
Left				

Muscle force/performance: Dynamometer:

Muscle	**Hip**				**Knee**		**Ankle**	
Force	*Fl*	*Ex*	*Abd*	*Add*	*Fl*	*Ex*	*Df*	*Pf*
Right-1								
2								
3								
Left-1								
2								
3								

ROM: Video- Silicon coach

Hip				Knee				Ankle				MT-P			
Flex		***Ext***		***Flex***		***Ext***		***Dflex***		***Pflex***		***Flex***		***Ext***	
R	**L**	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**

Photographs: AP, PA, ML, LM

Deformity	Equinus	Calcaneus	Pes planus	Pes cavus	Hallux valgus	Hammer toes	Mallet toes	Claw toes
Right								
Left								

One leg standing time: Applicable bilaterally to Groups A, C & D only.

Applicable unilaterally to Group B

(test only the limb without ulcer)

Trials	**RIGHT LOWER LIMB**	**LEFT LOWER LIMB**
	Eyes open (secs)	***Eyes open (secs)***
1		
2		
3		

LIST OF MEDICATIONS:

Research Centre for Clinical Kinaesiology

Foot/Lower limb function in diabetic neuropathy 2003

SUBJECT ID: ______________________________

DATE: ________________________________

Anthropometric measurements:	**Right (cm)**	**Left (cm)**
Greater trochanter to lateral epicondyle **(thigh length)**		
Knee joint line to the centre of the lateral malleolus		
Knee joint line to the floor **(knee height)**		
Heel to the longest toe (foot length)		
Malleolar width		
Knee width (condylar level)		

CHAIR HEIGHT: (0.1736 x thigh length) + knee height = ________________cm

Appendix 2

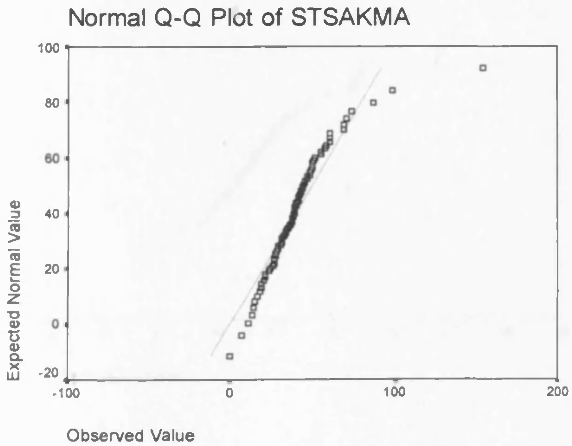
Appendix 2 includes the results demonstrating the normal distribution of the data from various outcome measures used to evaluate function. The data will follow the same sequence as the variables in the proposed model of function.

A2.1: Mobility:

A2.1a: Sit-to-stand:

The data from the net joint moments at the ankle, knee and hip on both the sides during the movement of STS showed normal distribution as demonstrated in the Figures. A2.1, A2.2 and A2.3 respectively.

Figure A2.1: Normal distribution of the data from the net joint moments of the ankle on the affected side (left) and the contra-lateral limb (right) during STS movement.



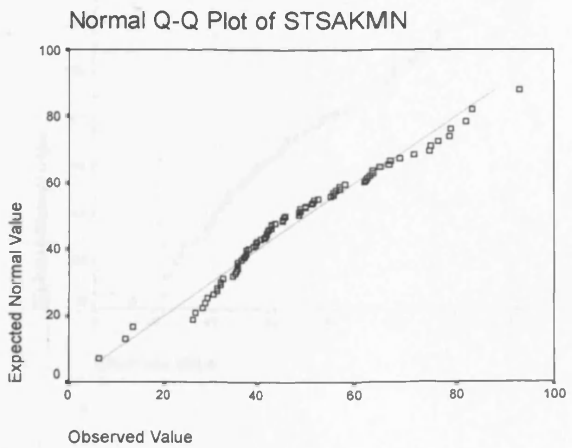


Figure A2.2: Normal distribution of the data from the net joint moments of the knee on the affected limb (left) and on the contra-lateral limb (right) during STS movement

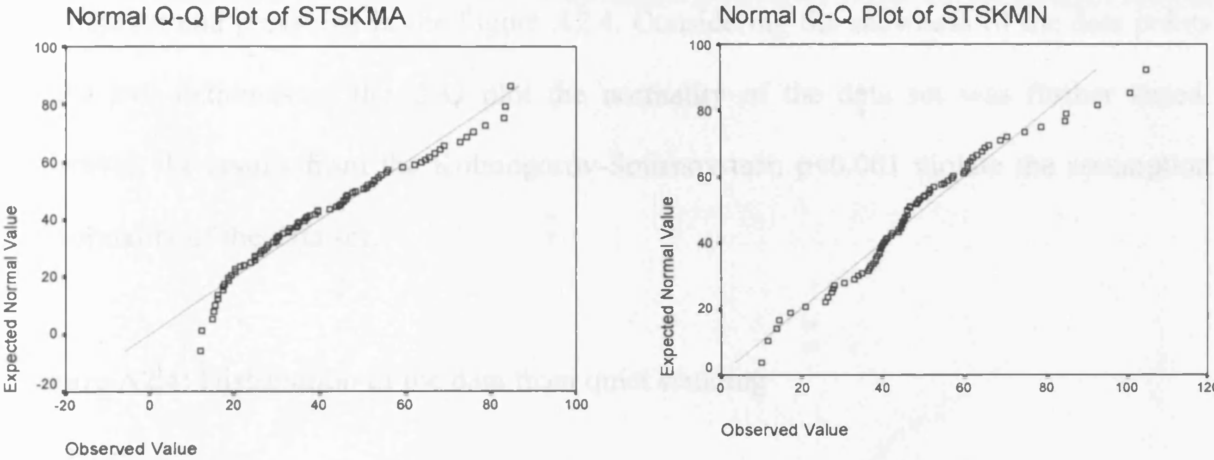
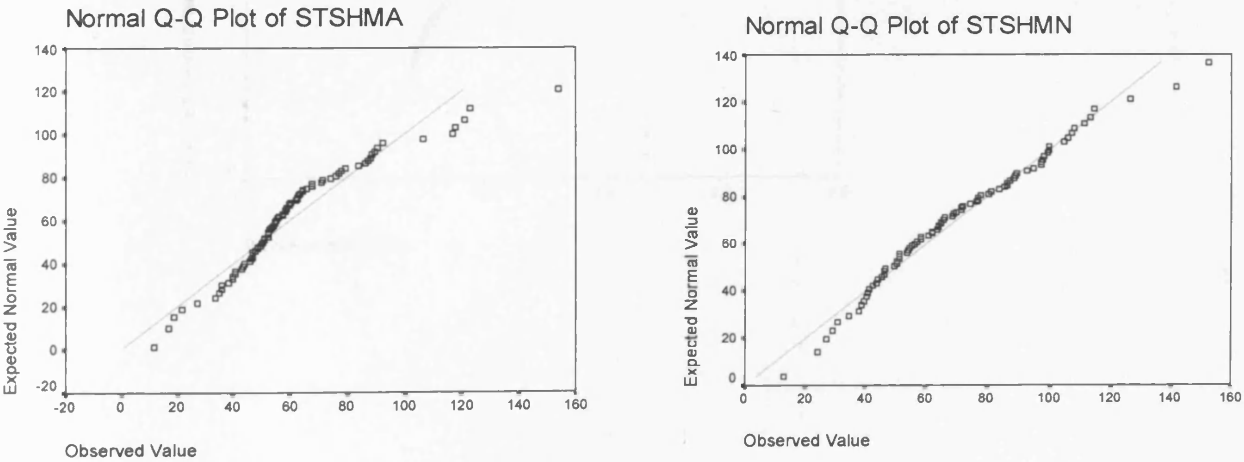


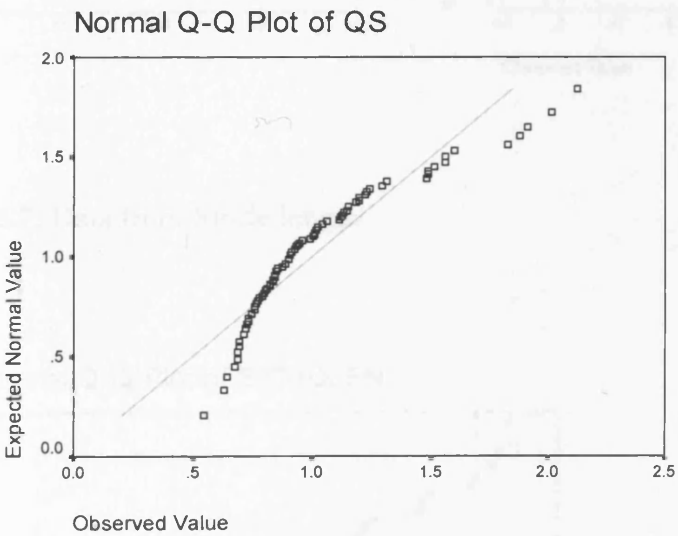
Figure A2.3: Normal distribution of the data from the net joint moments of the hip on the affected limb (left) and on the contra-lateral limb (right) during STS movement



A2.1b: Quiet standing:

The distribution of the data from all the 4 groups for quiet standing was tested for normal distribution and presented in the Figure A2.4. Considering the skewness of the data points at the two extremes of the Q-Q plot the normality of the data set was further tested. However, the results from the Kolmogorov-Smirnov test: $p<0.001$ violate the assumption of normality of the data set.

Figure A2.4: Distribution of the data from quiet standing



A2.1c: Gait:

Data from cadence, gait velocity and stride length were distributed normally as presented in the Figures A2.5-A2.7.

Figure A2.5: Data from Cadence

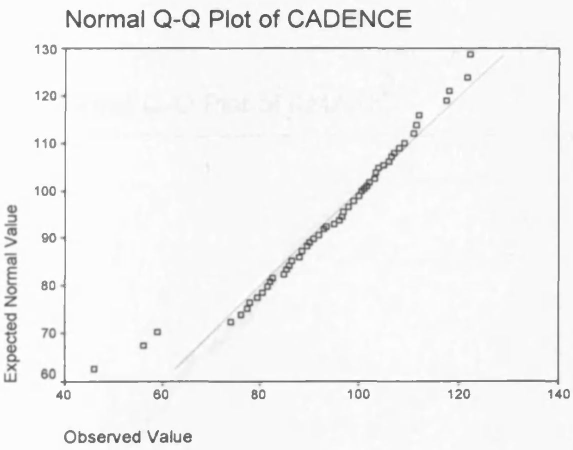


Figure A2.6: Data from Gait velocity

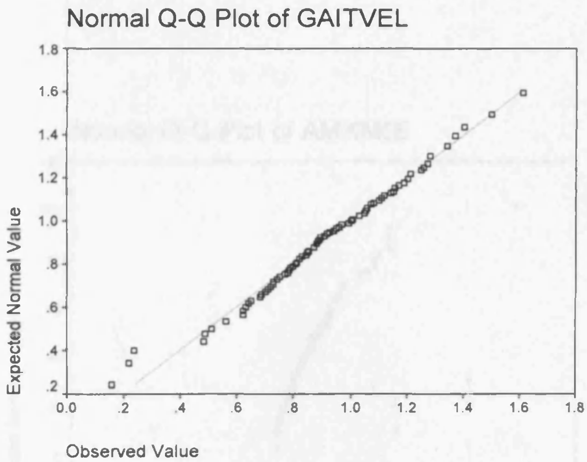
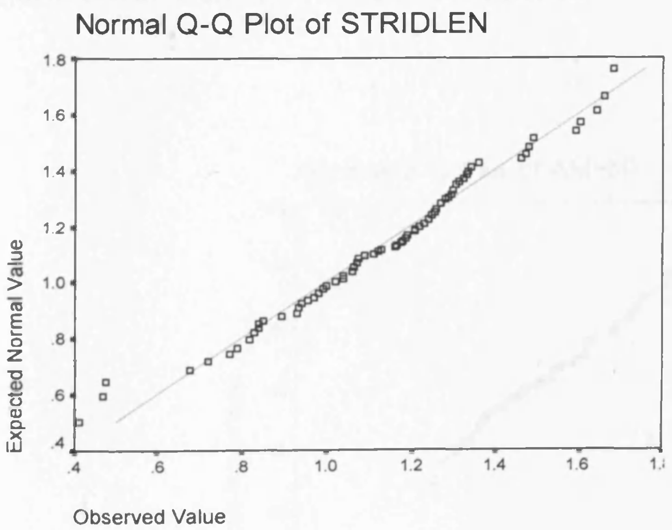


Figure A2.7: Data from Stride length



Net joint moments during walking: The data from the ankle, knee and hip joint moments during gait on the affected limb from all the four groups were distributed normally as seen in the figures below (A2.8-A2.10).

Figure A2.8: Data from affected ankle moment

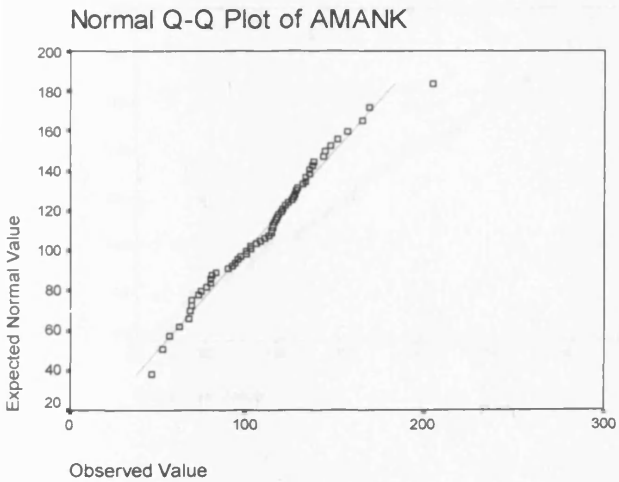


Figure A2.9: Data from affected knee moment

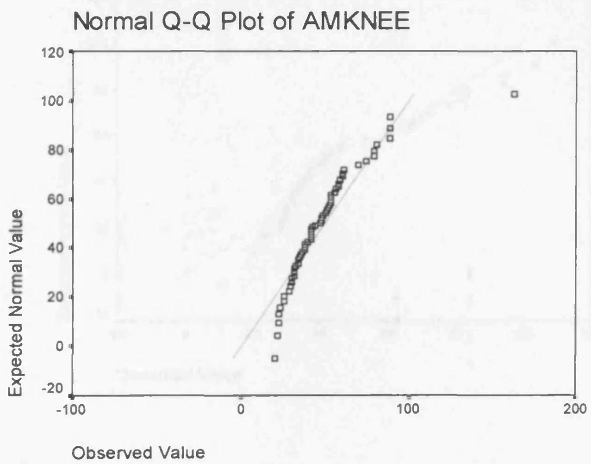
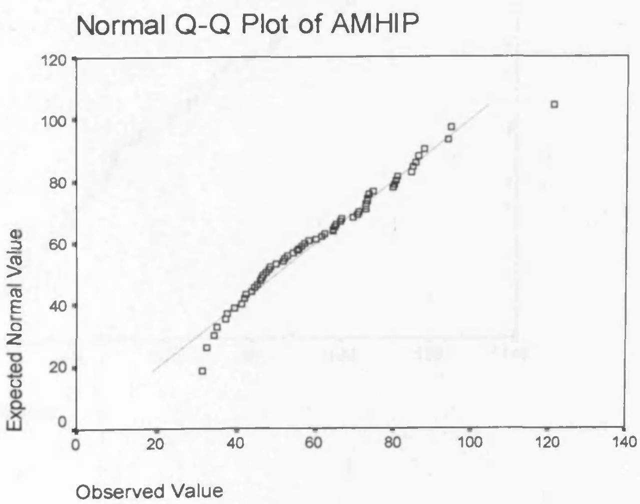


Figure A2.10: Data from affected hip moment



The data from the ankle, knee and hip joint moments during gait on the contra-lateral limb from all the four groups were distributed normally as seen in the Figures below (A2.11-A2.13).

Figure A2.11: Data from contra-lateral ankle moment

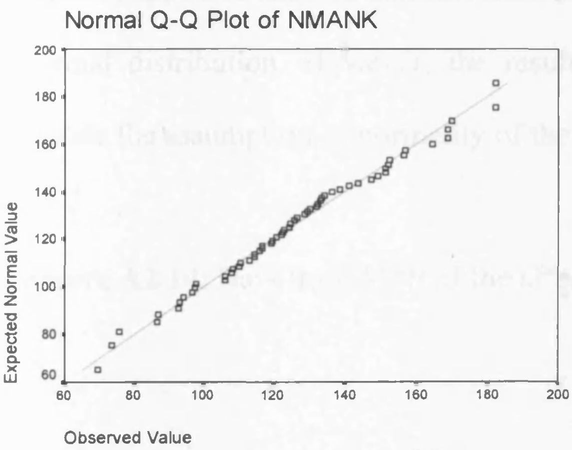


Figure A2.12: Data from contra-lateral knee moment

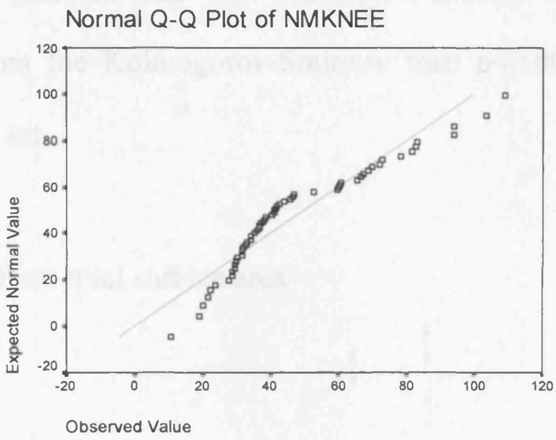
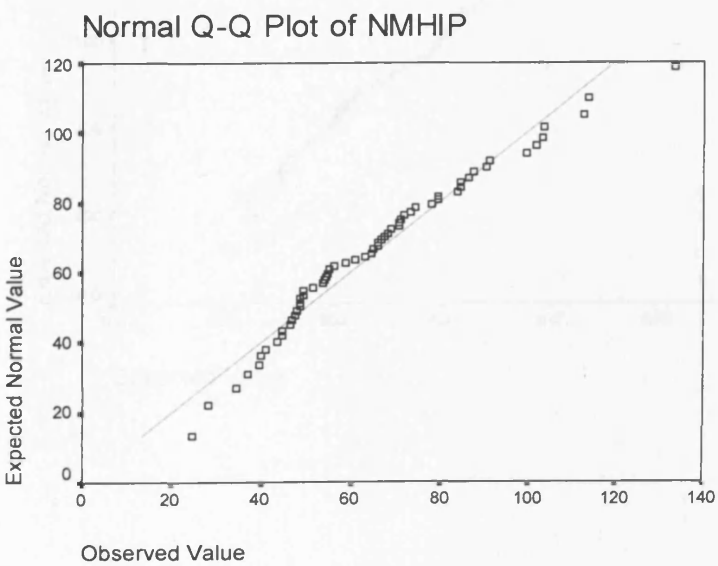


Figure A2.13: Data from contra-lateral hip moment



A2.2: Plantar pressure distribution:

Peak plantar pressures (MPP):

Affected foot: The data from peak plantar pressures (MPP) over the affected foot met the requirements for normal distribution. Figure A2.14 demonstrates the distribution of the data from MPP of the affected foot: total surface area. Figure A2.15 demonstrates the distribution of the data from MPP of the 6 regions of the foot. The data from the affected midfoot appeared skewed and therefore Kolmogorov-Smirnov test was used to confirm the normal distribution. However, the results from the Kolmogorov-Smirnov test: $p<0.001$ violate the assumption of normality of the data set.

Figure A2.14: Data from MPP of the affected foot: total surface area

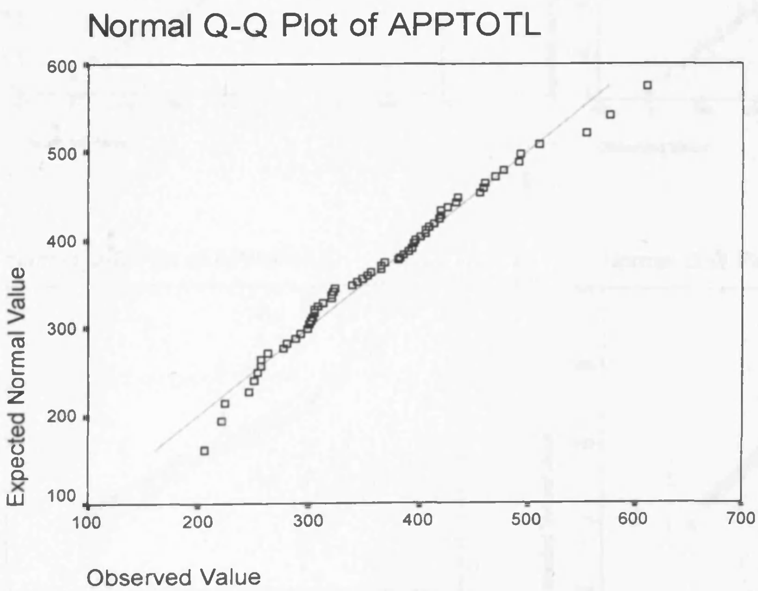
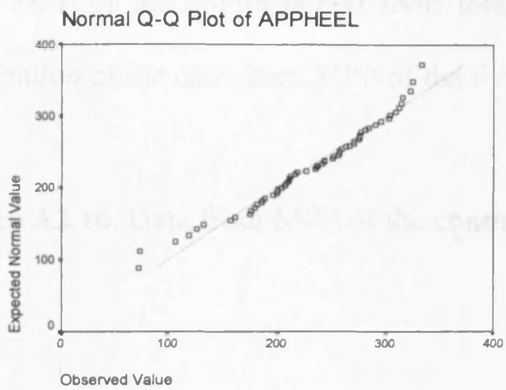


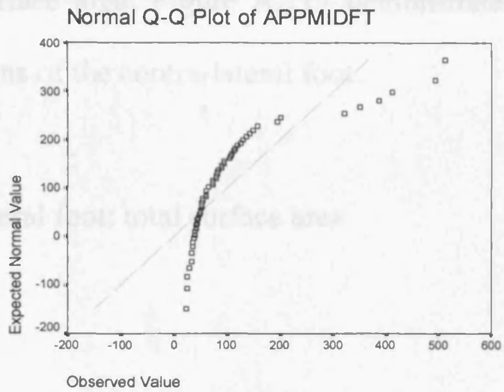
Figure A2.15: Data from MPP of the 6 regions of the affected foot:

A: Heel, **B:** Midfoot, **C:** 1-2 MTP region, **D:** 3-4-5 MTP region, **E:** Hallux, **F:** Toes

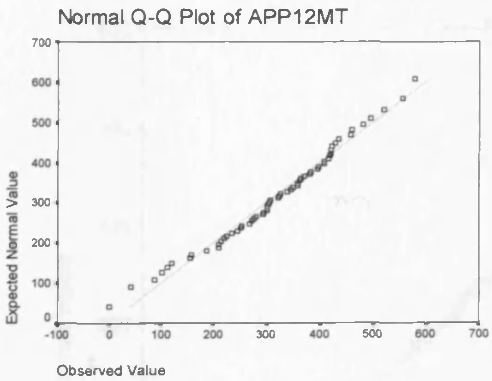
A



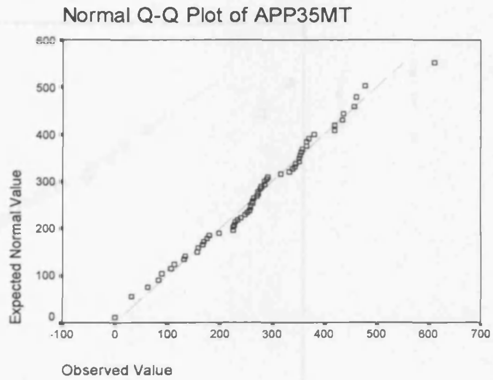
B



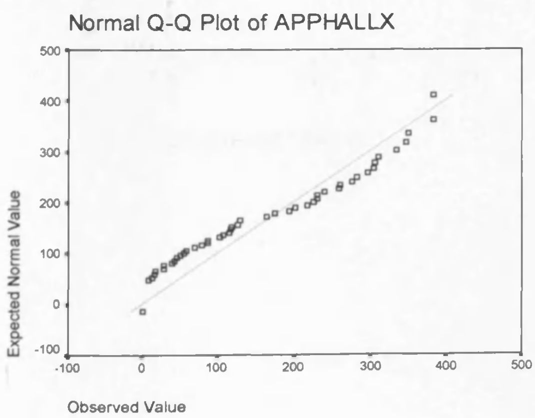
C



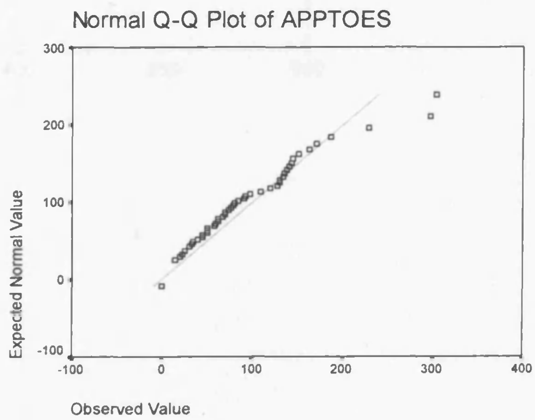
D



E



F



Contra-lateral foot:

The data from peak plantar pressures (MPP) over the contra-lateral foot met the requirements for normal distribution. Figure A2.16 demonstrates the distribution of the data from MPP of the contra-lateral foot: total surface area. Figure A2.17 demonstrates the distribution of the data from MPP of the 6 regions of the contra-lateral foot.

Figure A2.16: Data from MPP of the contra-lateral foot: total surface area

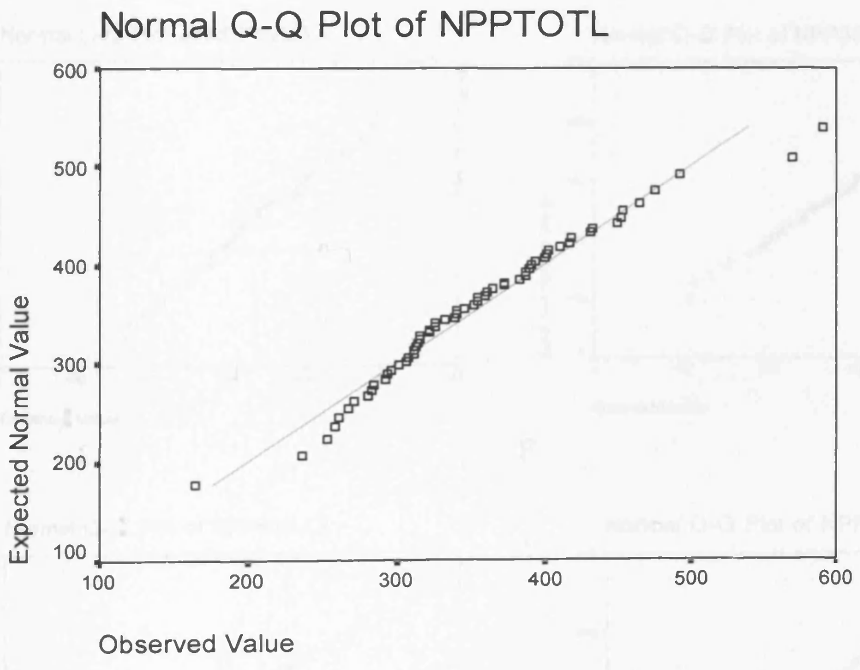
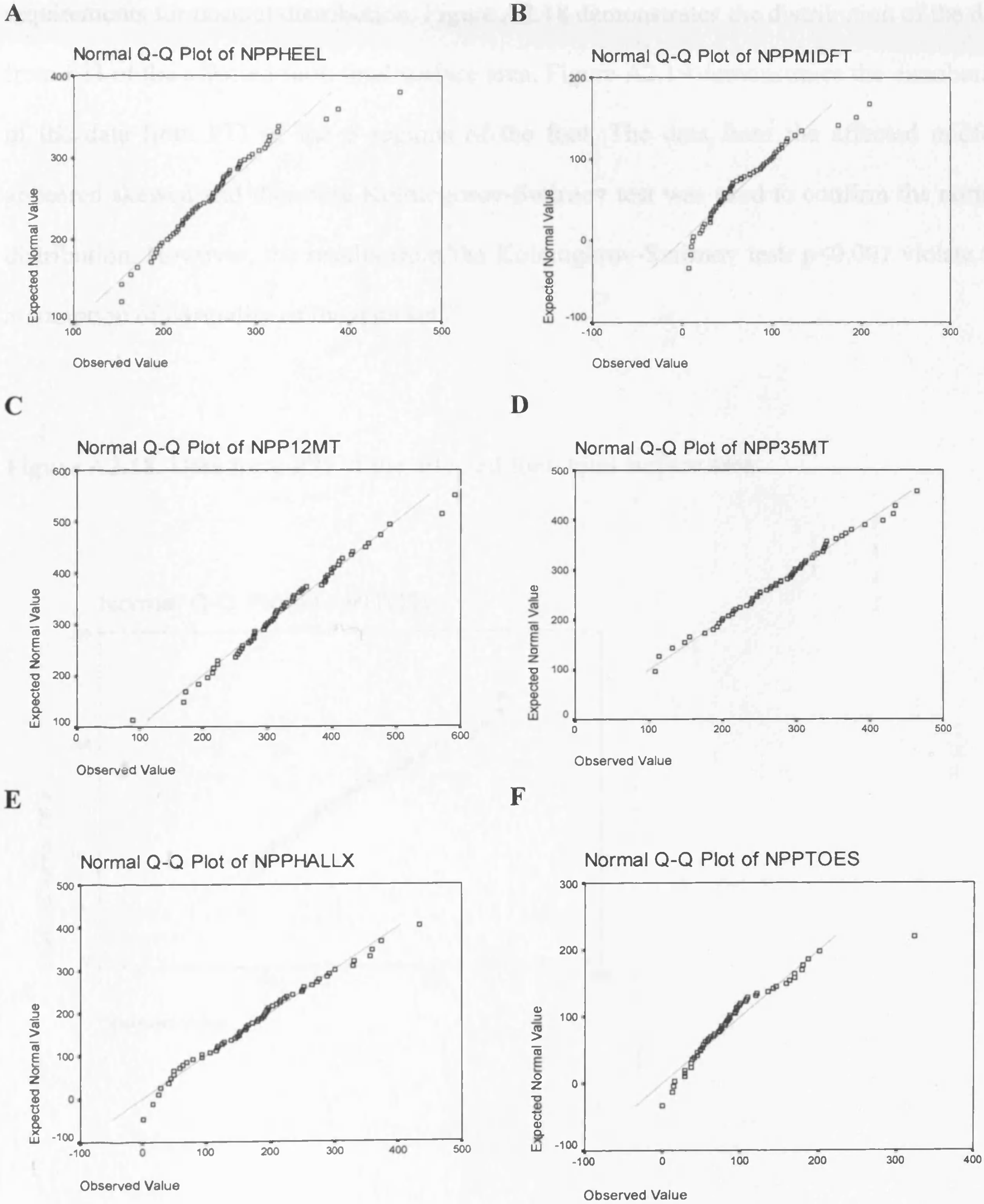


Figure A2.17: Data from MPP of the 6 regions of the contra-lateral foot:

A: Heel, **B:** Midfoot, **C:** 1-2 MTP region, **D:** 3-4-5 MTP region, **E:** Hallux, **F:** Toes



Pressure-time integral (PTI):

Affected foot: The data from pressure-time integral over the affected foot met the requirements for normal distribution. Figure A2.18 demonstrates the distribution of the data from PTI of the affected foot: total surface area. Figure A2.19 demonstrates the distribution of the data from PTI of the 6 regions of the foot. The data from the affected midfoot appeared skewed and therefore Kolmogorov-Smirnov test was used to confirm the normal distribution. However, the results from the Kolmogorov-Smirnov test: $p<0.001$ violate the assumption of normality of the data set.

Figure A2.18: Data from PTI of the affected foot: total surface area

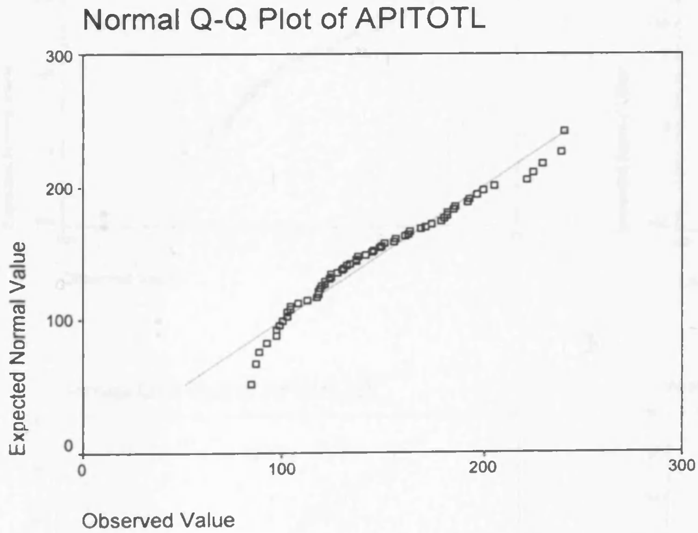
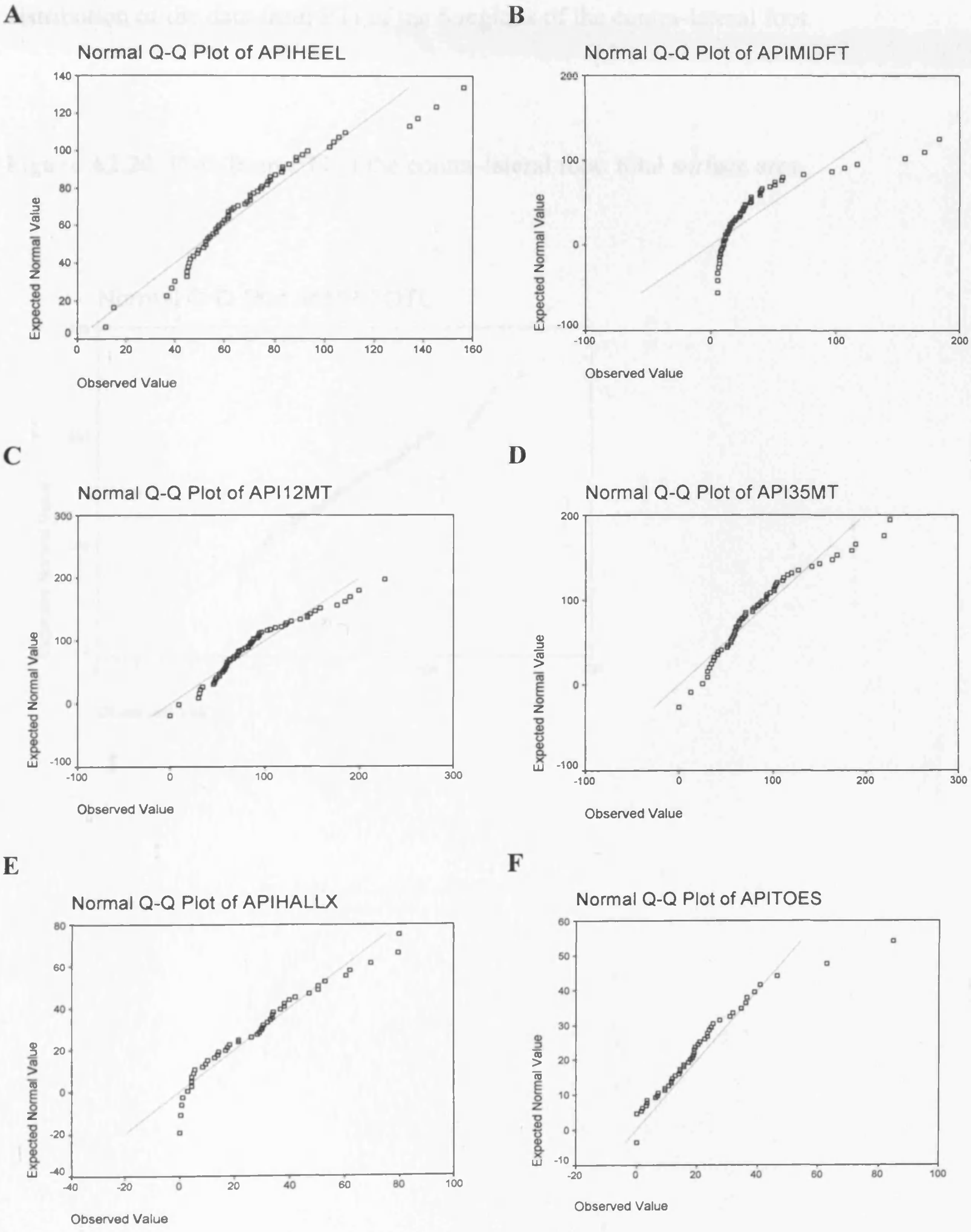


Figure A2.19: Data from PTI of the 6 regions of the affected foot:

A: Heel, **B:** Midfoot, **C:** 1-2 MTP region, **D:** 3-4-5 MTP region, **E:** Hallux, **F:** Toes



Contra-lateral foot: The data from pressure-time integral over the contra-lateral foot met the requirements for normal distribution. Figure A2.20 demonstrates the distribution of the data from PTI of the contra-lateral foot: total surface area. Figure A2.21 demonstrates the distribution of the data from PTI of the 6 regions of the contra-lateral foot.

Figure A2.20: Data from PTI of the contra-lateral foot: total surface area

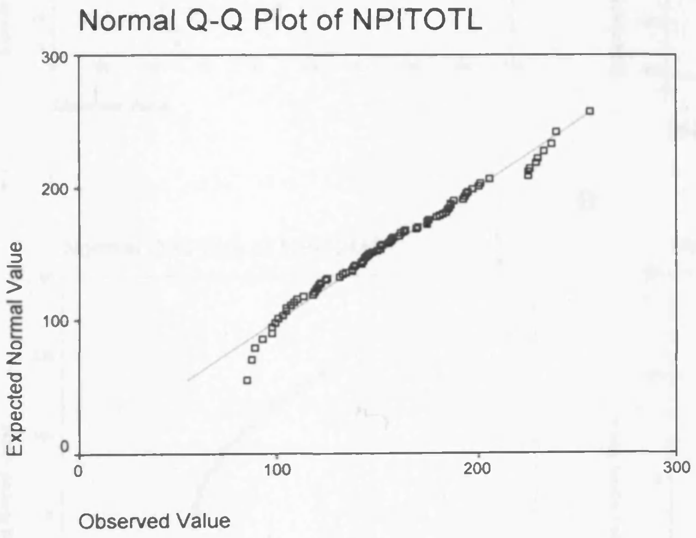
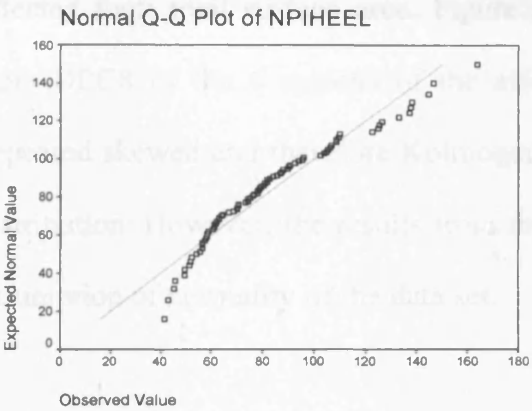


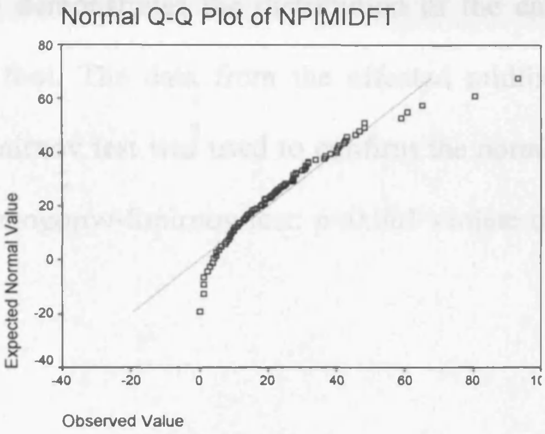
Figure A2.21: Data from PTI of the 6 regions of the contra-lateral foot:

A: Heel, **B:** Midfoot, **C:** 1-2 MTP region, **D:** 3-4-5 MTP region, **E:** Hallux, **F:** Toes

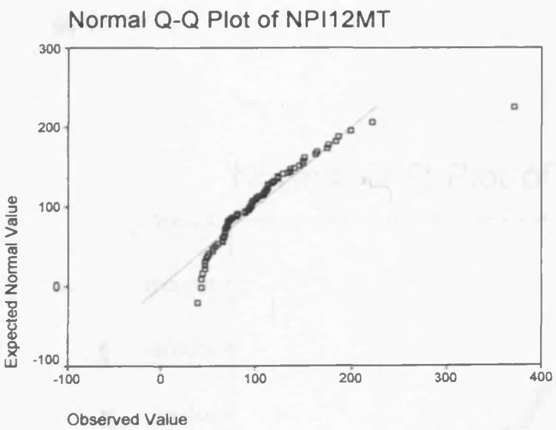
A



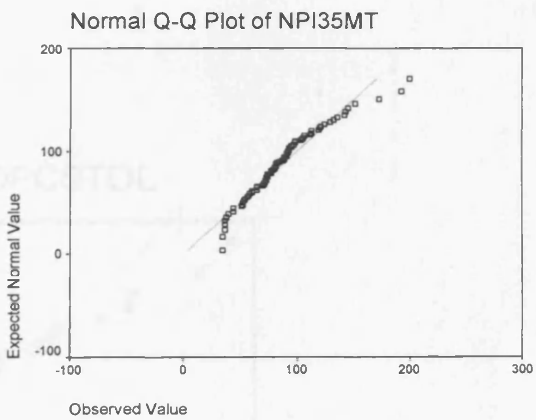
B



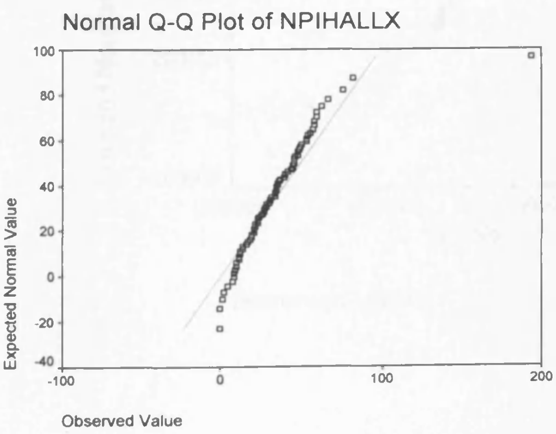
C



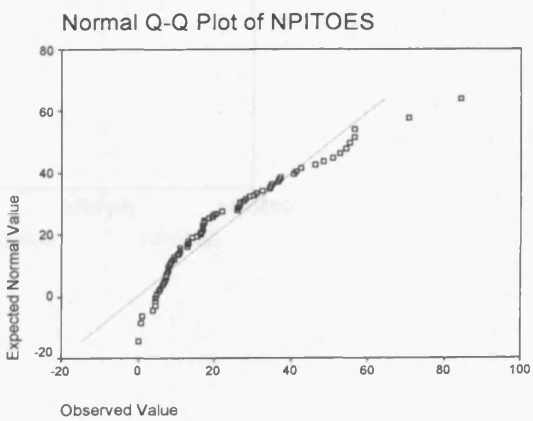
D



E



F



Daily plantar cumulative stress (DPCS):

Affected foot: The data from DPCS over the affected foot met the requirements for normal distribution. Figure A2.22 demonstrates the distribution of the data from DPCS of the affected foot: total surface area. Figure A2.23 demonstrates the distribution of the data from DPCS of the 6 regions of the affected foot. The data from the affected midfoot appeared skewed and therefore Kolmogorov-Smirnov test was used to confirm the normal distribution. However, the results from the Kolmogorov-Smirnov test: $p<0.001$ violate the assumption of normality of the data set.

Figure A2.22: Data from DPCS of the affected foot: total surface area

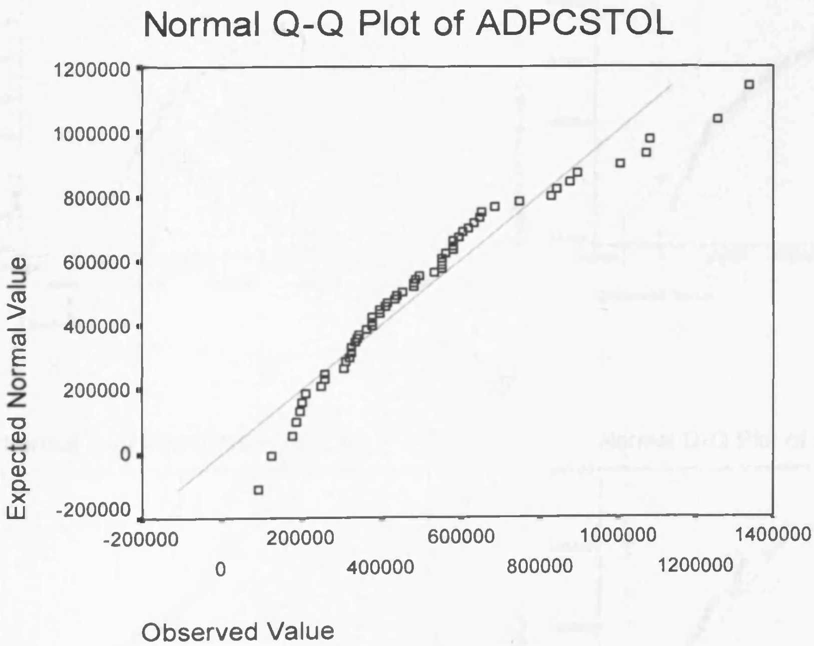
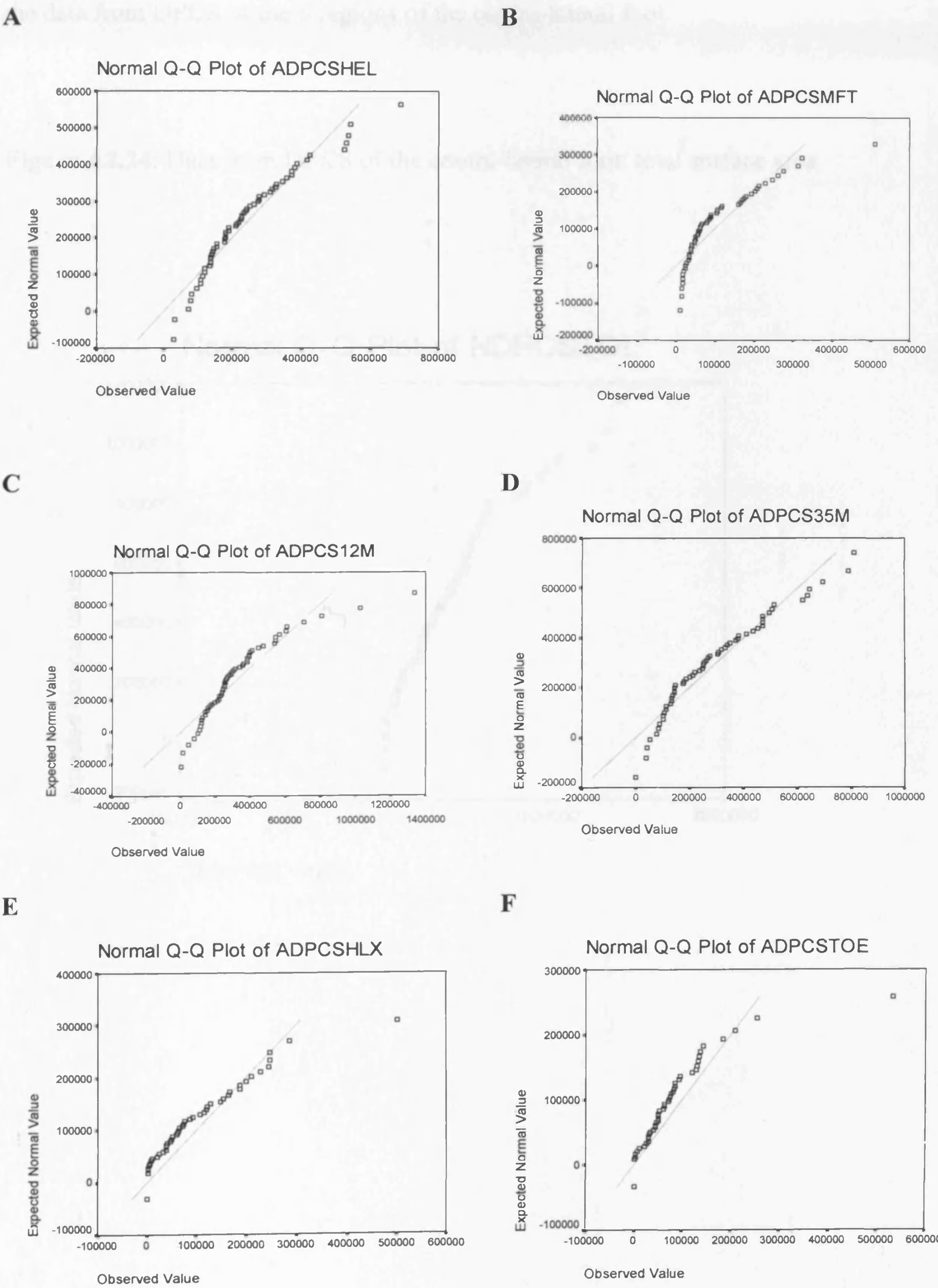


Figure A2.23: Data from DPCS of the 6 regions of the affected foot:

A: Heel, **B:** Midfoot, **C:** 1-2 MTP region, **D:** 3-4-5 MTP region, **E:** Hallux, **F:** Toes



Contra-lateral foot: The data from DPCS over the contra-lateral foot met the requirements for normal distribution. Figure A2.24 demonstrates the distribution of the data from DPCS of the contra-lateral foot: total surface area. Figure A2.25 demonstrates the distribution of the data from DPCS of the 6 regions of the contra-lateral foot.

Figure A2.24: Data from DPCS of the contra-lateral foot: total surface area

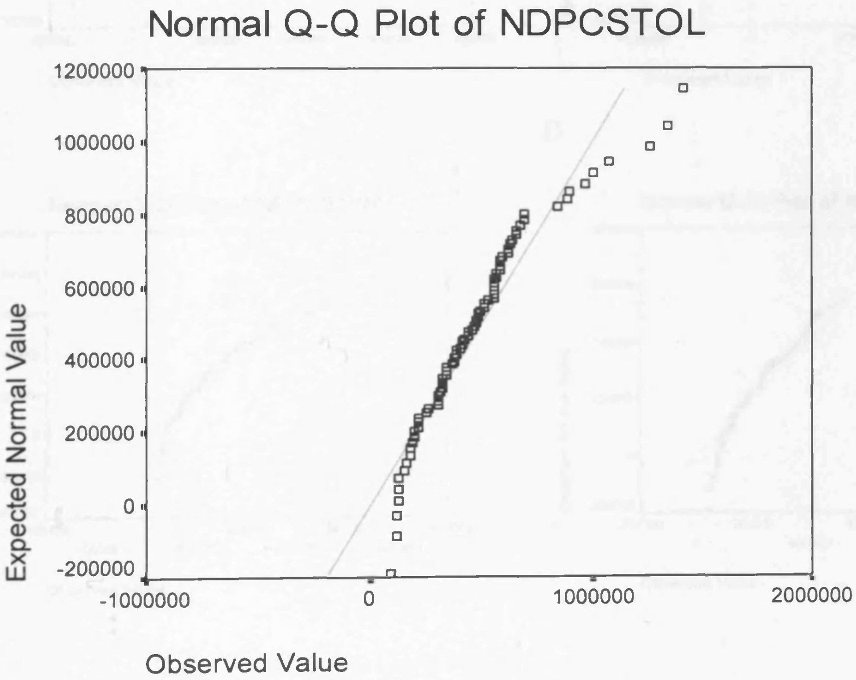
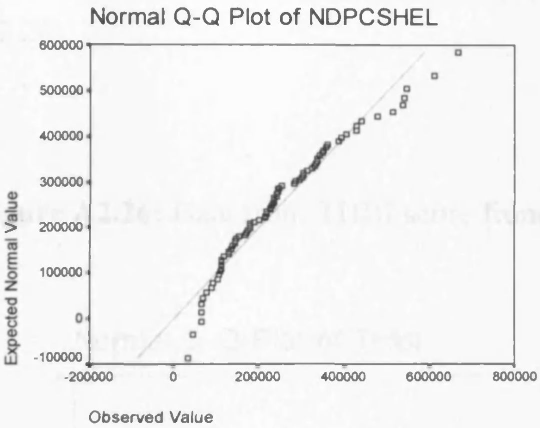


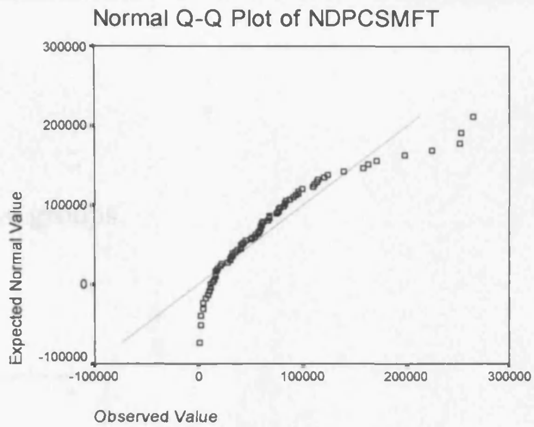
Figure A2.25: Data from DPCS of the 6 regions of the contra-lateral foot:

A: Heel, **B:** Midfoot, **C:** 1-2 MTP region, **D:** 3-4-5 MTP region, **E:** Hallux, **F:** Toes

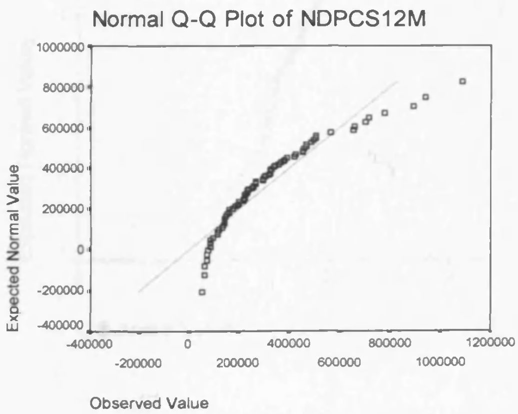
A



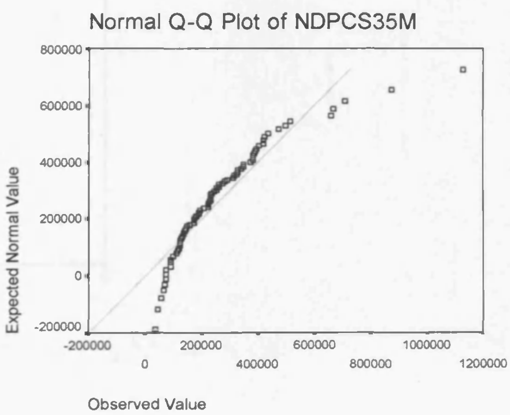
B



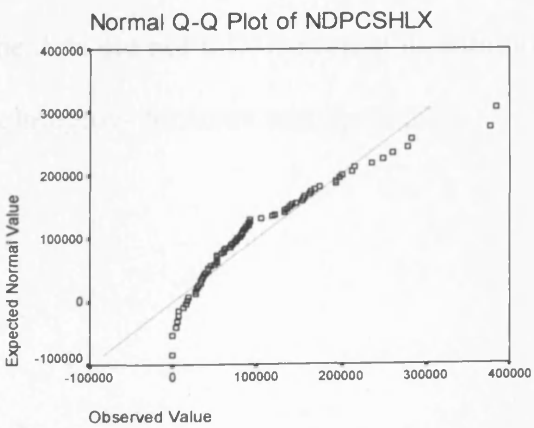
C



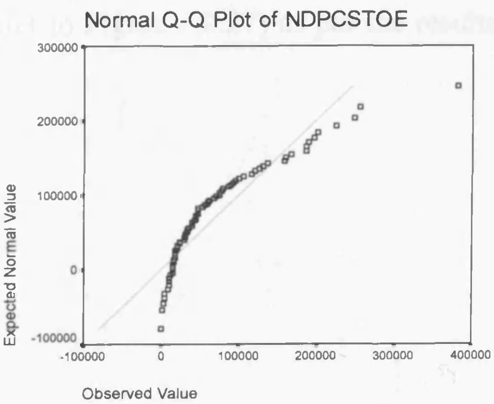
D



E



F

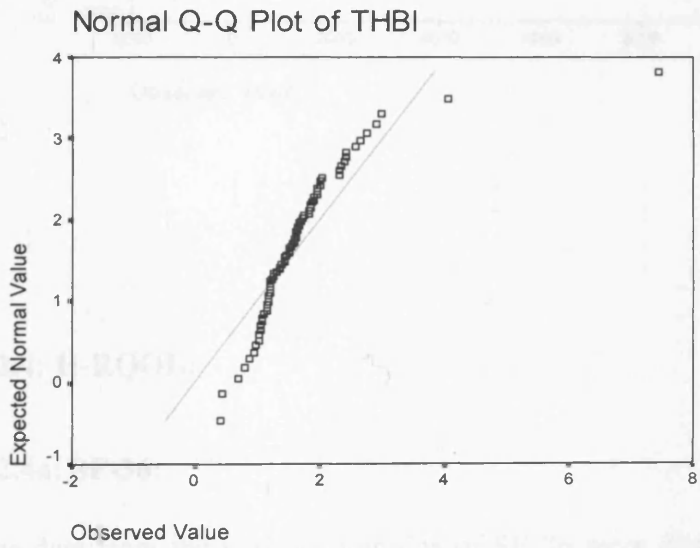


A2.3: Activity level:

A2.3a: Capacity: Total Heart Beat Index (THBI):

The data from THBI score met the requirements for normal distribution (refer to Figure A2.26).

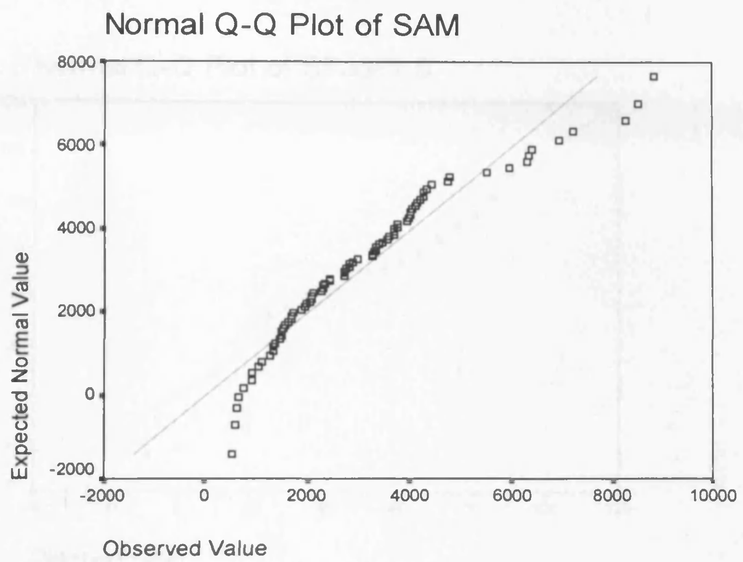
Figure A2.26: Data from THBI score from all 4 groups



A2.3b: Performance: Average daily strides:

The data did not follow normal distribution (refer to Figure A2.27) as per the results of the Kolmogrov- Smirnov test. (p=0.022).

Figure A2.27: Data from average daily strides from all 4 groups



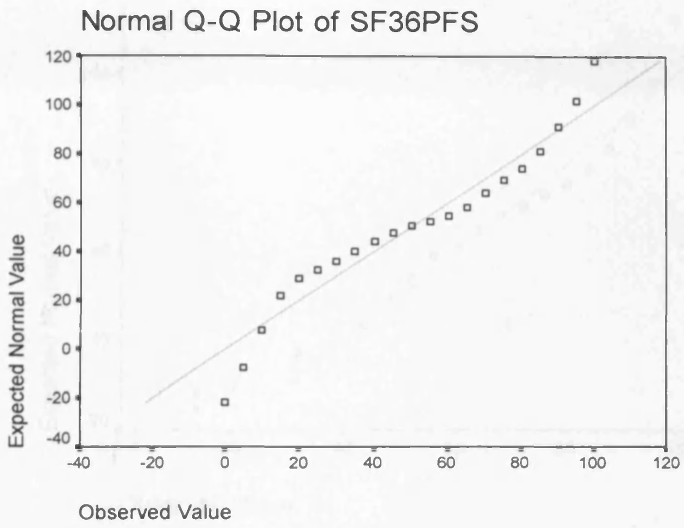
A2.4: H-RQOL:

A2.4a: SF-36:

The data from the various domains of SF-36 were distributed normally except the domain of physical function (Kolmogorov-Smirnov test: p=0.007).

The Q-Q plots demonstrating the distribution of the data (refer to Figures A2.28 to A2.36) are presented.

Figure A2.28: Data from SF-36 Physical function Score



Social function:

Figure A2.29: Data from SF-36 Social function Score

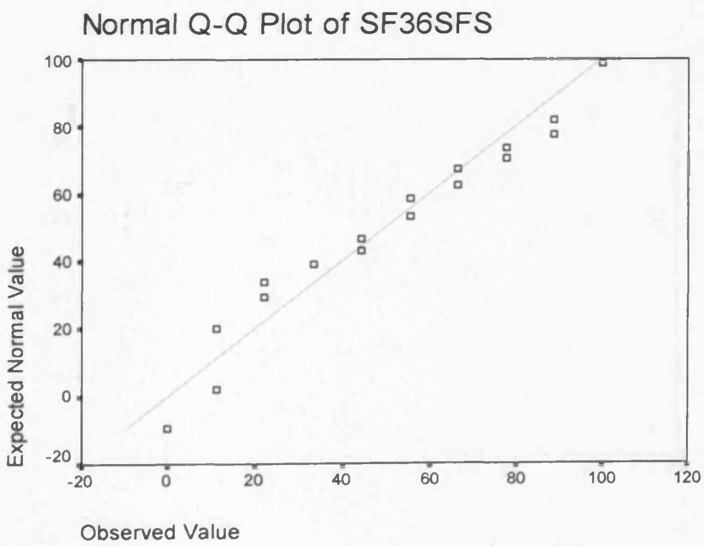


Figure A2.30: Data from SF-36 Mental health Score

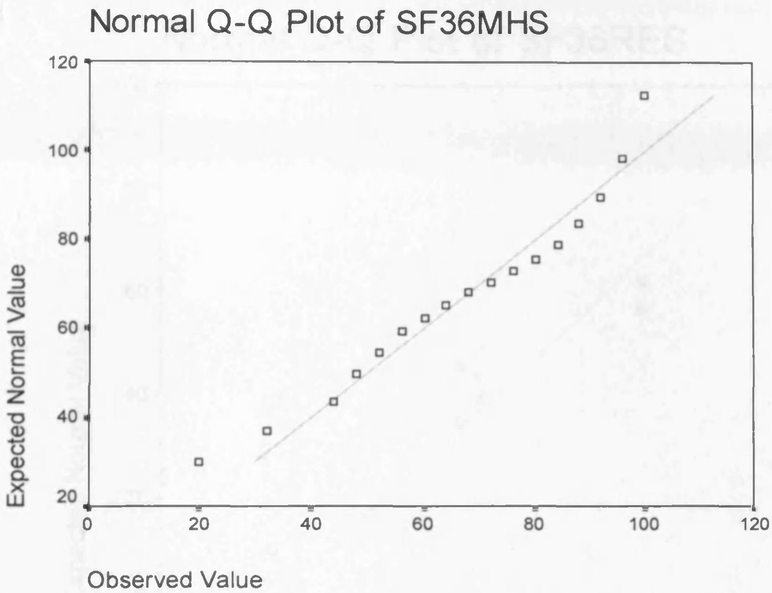


Figure A2.31: Data from SF-36 Role limitation due to physical problems Score

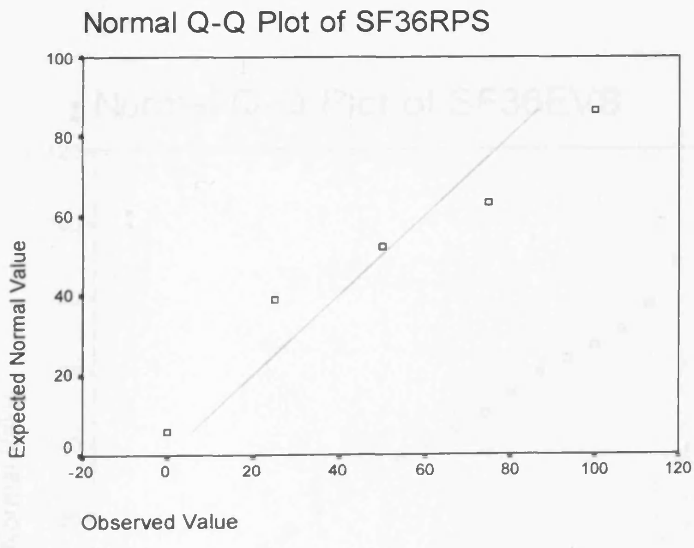


Figure A2.32: Data from SF-36 Role limitation due to emotional problems Score

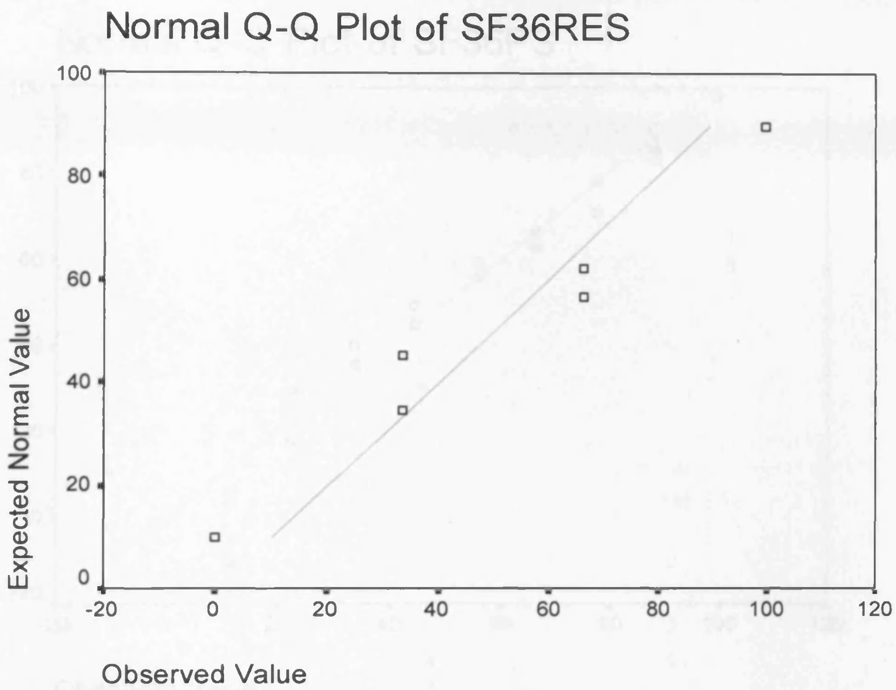


Figure A2.33: Data from SF-36 Energy Vitality Score

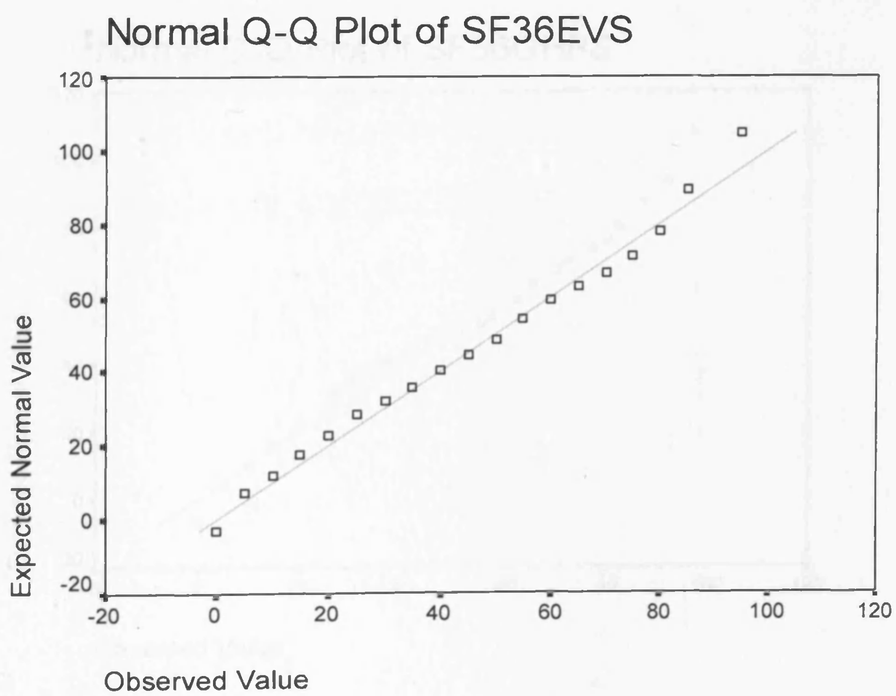


Figure A2.34: Data SF-36 from Pain Score

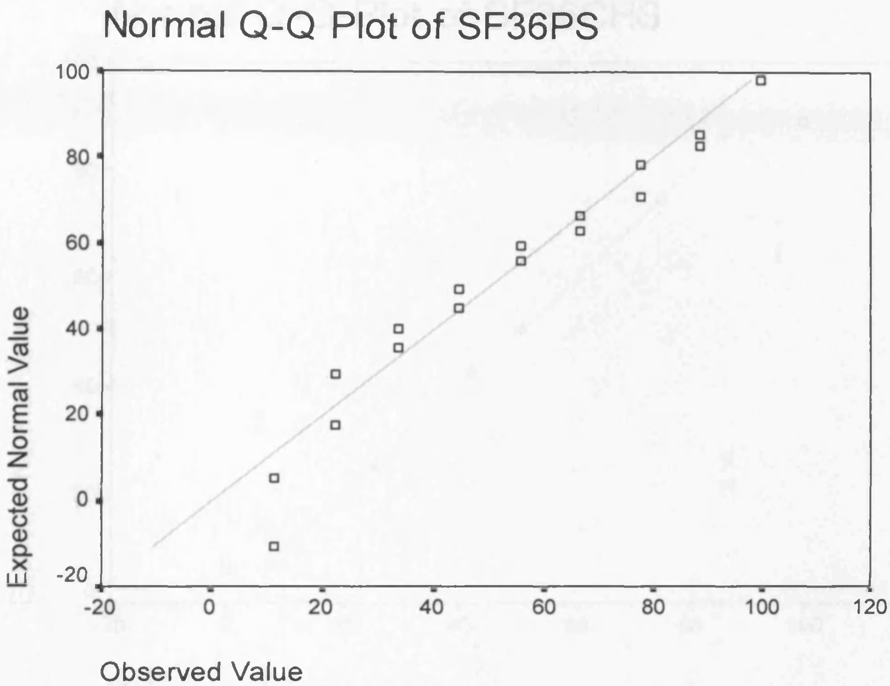


Figure A2.35: Data from SF-36 General Health Perception Score

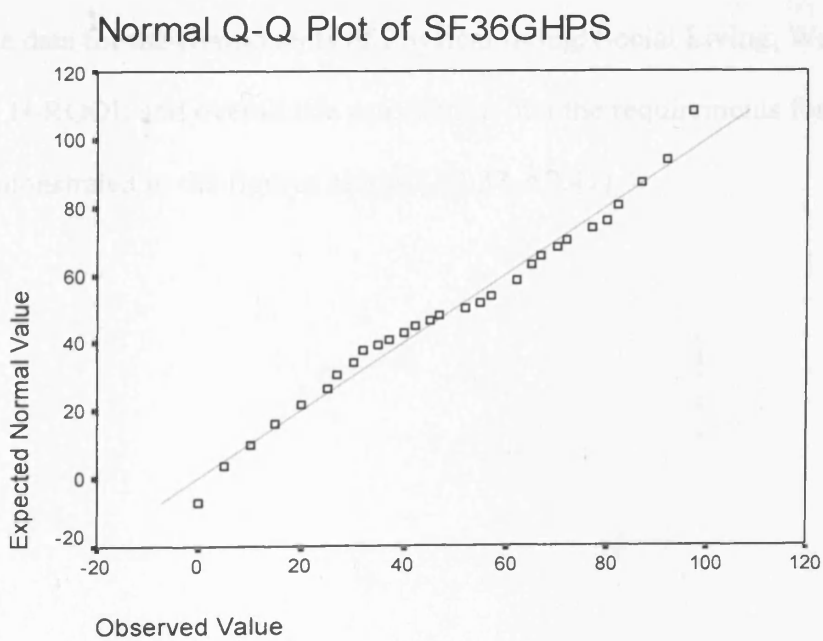
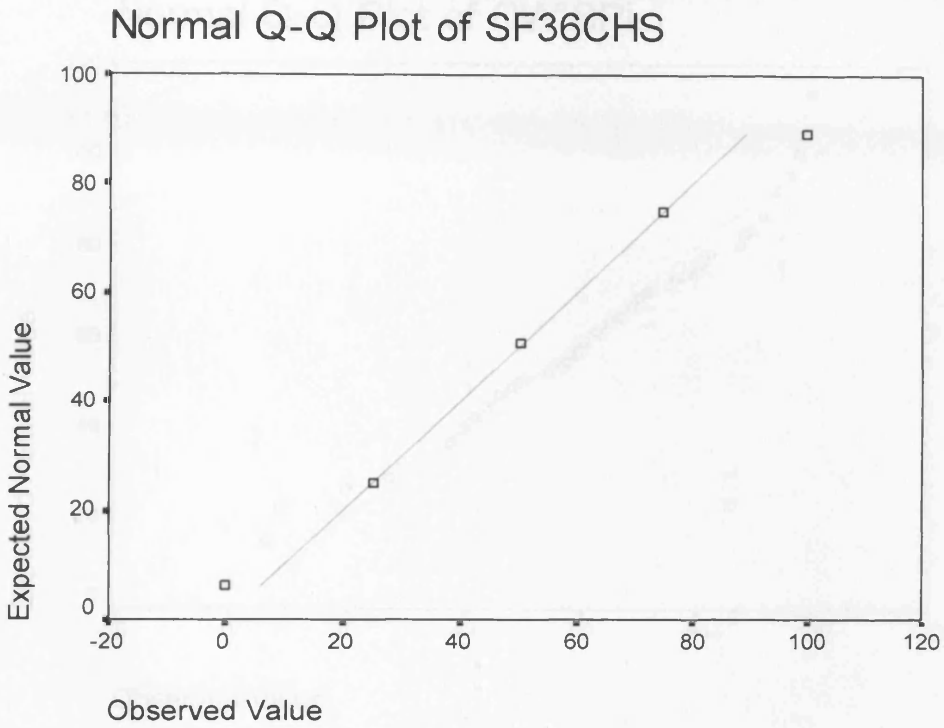


Figure A2.36: Data from SF-36 Change in Health Status Score



A2.4b: Cardiff Wound Impact Scale (CWIS):

The data for the components of Physical living, Social Living, Well-being and global scales for H-RQOL and overall life satisfaction met the requirements for normal distribution as demonstrated in the figures below (A2.37-A2.41).

Figure A2.37: Data from CWIS: Physical Living Score

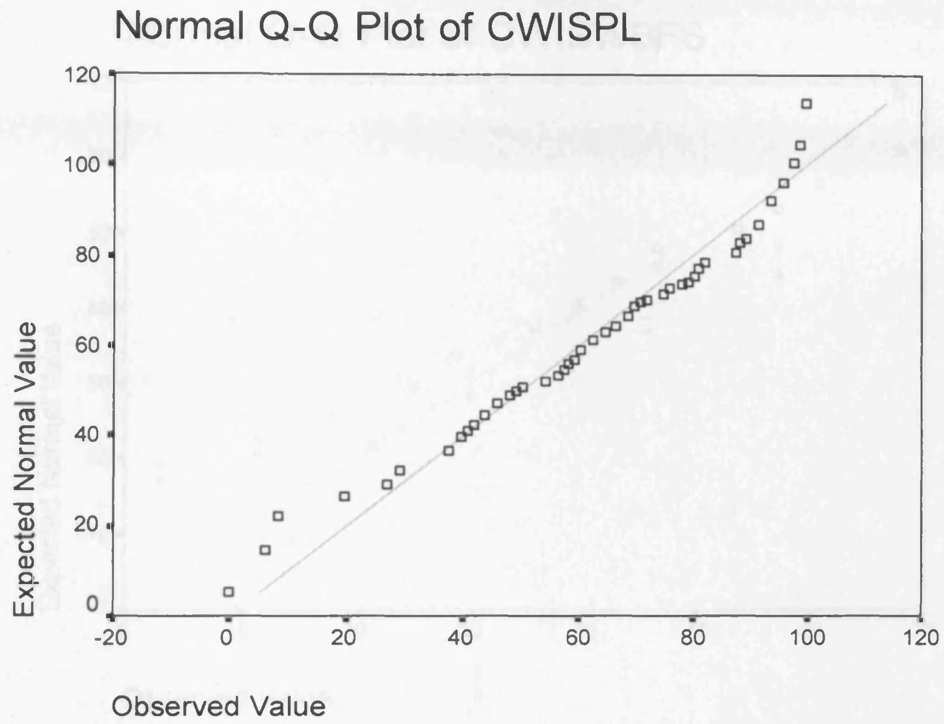


Figure A2.38: Data from CWIS: Social Living Score

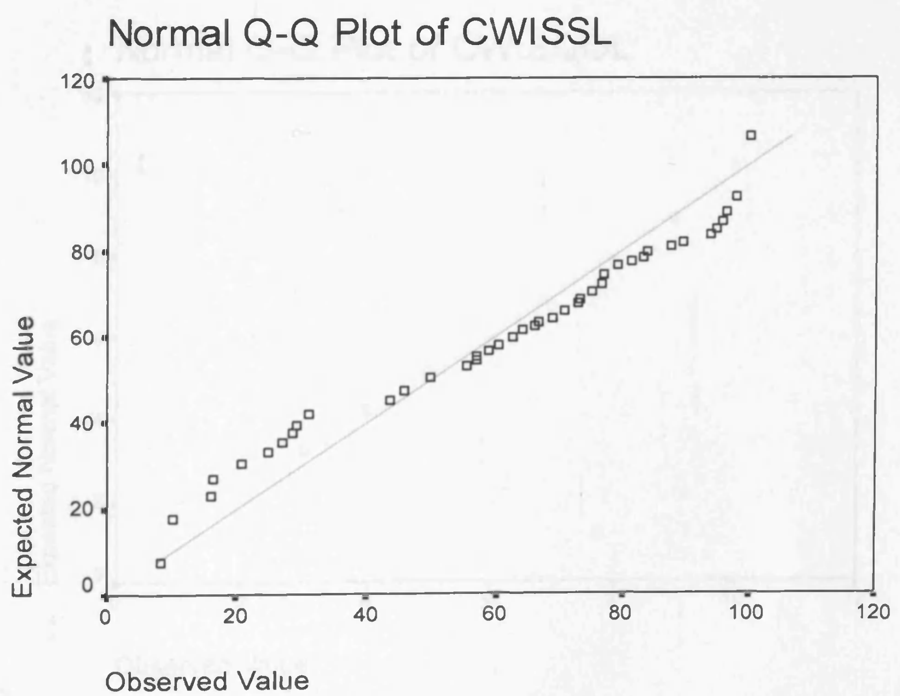


Figure A2.39: Data from CWIS: Well-being Score

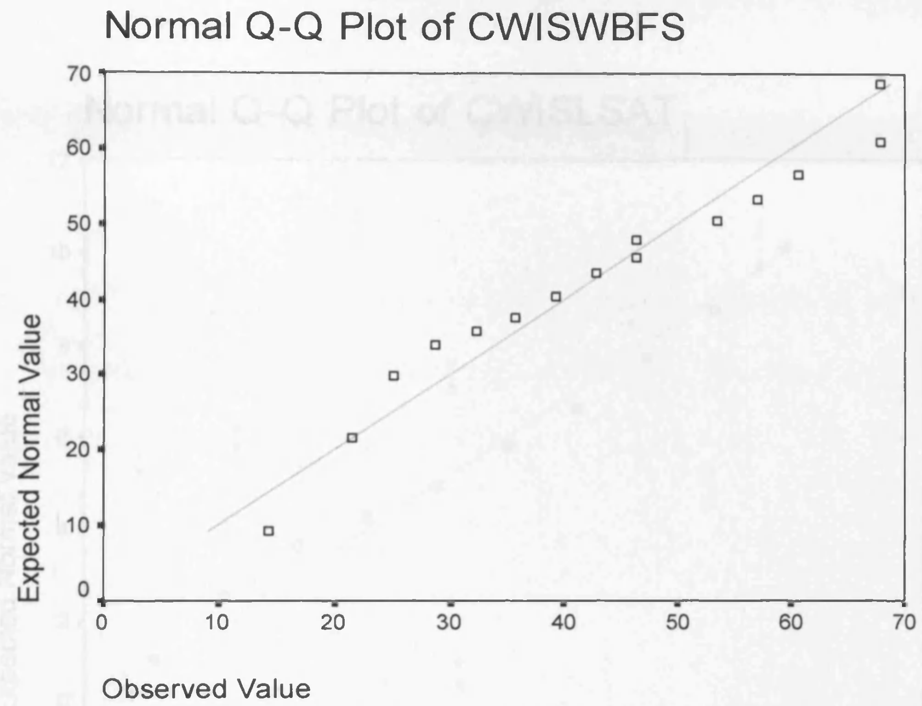


Figure A2.40: Data from CWIS: H-RQOL Score

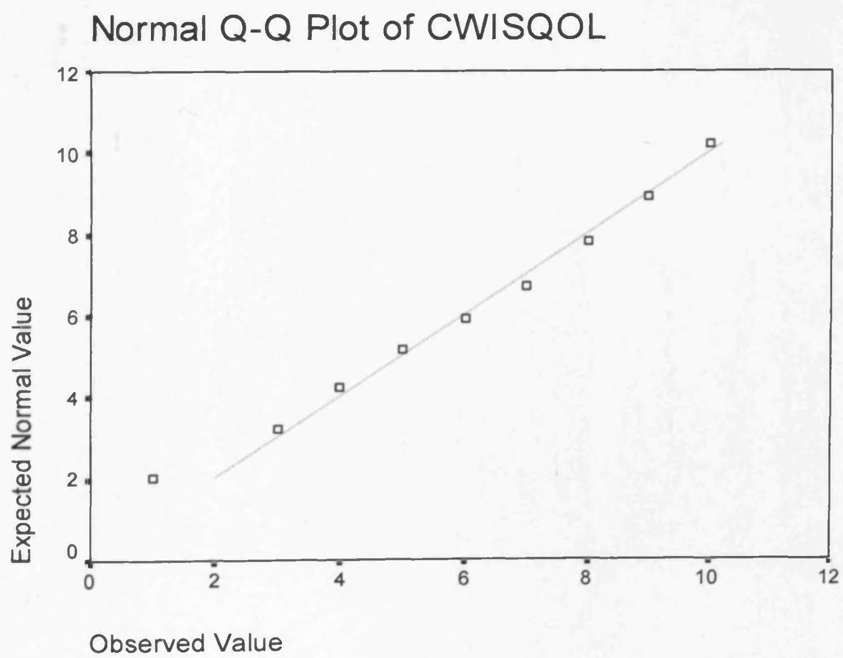
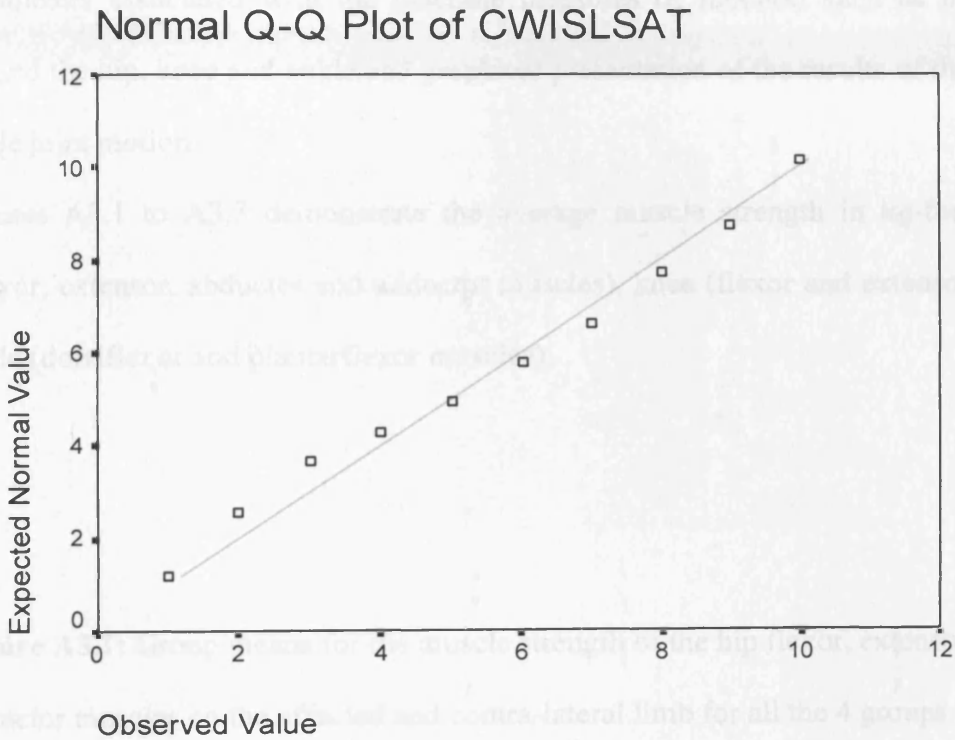


Figure A2.41: Data from CWIS: Life satisfaction Score



Appendix 3

Appendix 3 includes the graphical and tabular presentation of the results from the parameters associated with the outcome measures of function such as muscle strength around the hip, knee and ankle and graphical presentation of the results of the hip, knee and ankle joint motion.

Figures A3.1 to A3.3 demonstrate the average muscle strength in kg-force for the hip (flexor, extensor, abductor and adductor muscles), knee (flexor and extensor muscles) and ankle (dorsiflexor and plantarflexor muscles).

Figure A3.1: Group means for the muscle strength of the hip flexor, extensor, abductor and adductor muscles on the affected and contra-lateral limb for all the 4 groups

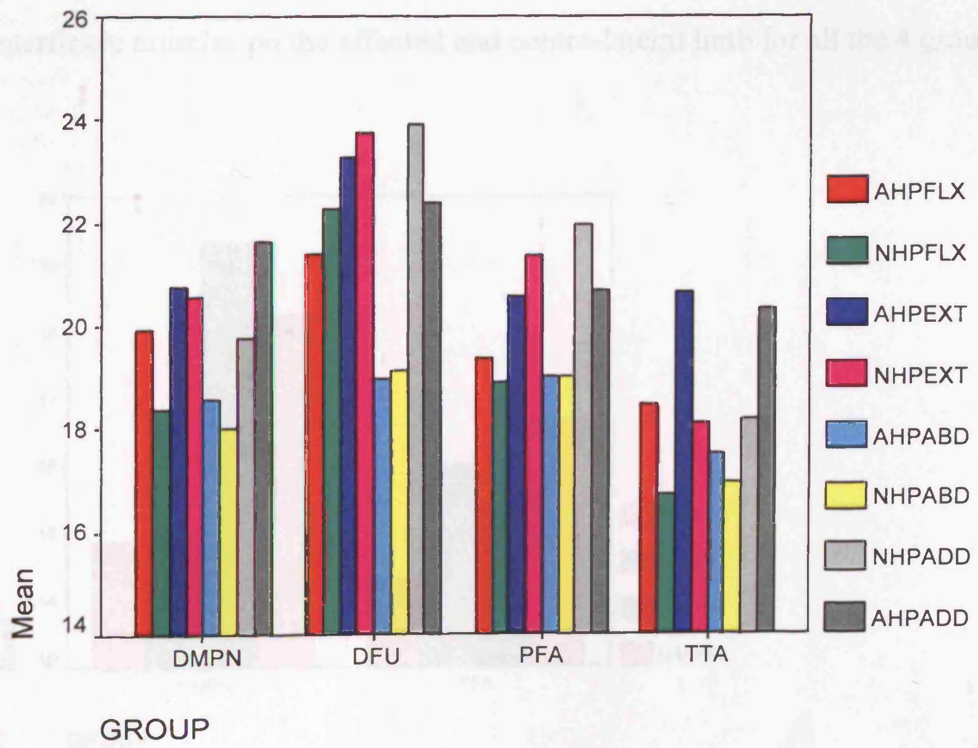


Figure A3.2: Group means for the muscle strength of the knee flexor and extensor muscles on the affected and contra-lateral limb for all the 4 groups

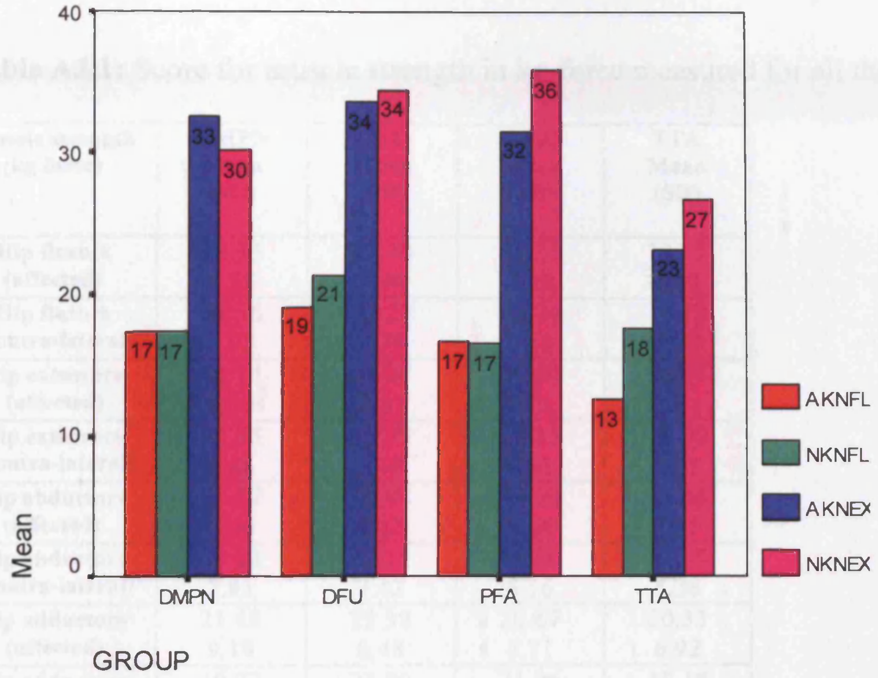
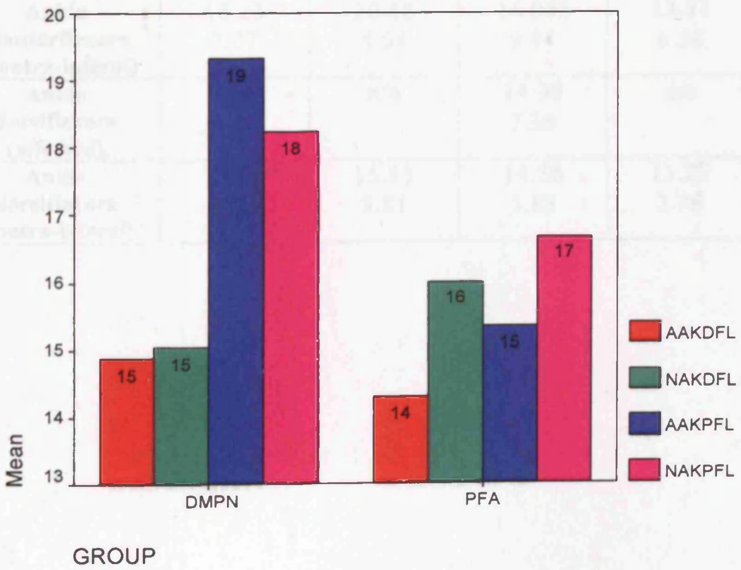


Figure A3.3: Group means for the muscle strength of the ankle dorsiflexor and plantarflexor muscles on the affected and contra-lateral limb for all the 4 groups



The table A3.1 presents the score for muscle strength in kg force measured for all the 4 groups.

Table A3.1: Score for muscle strength in kg-force measured for all the 4 groups

Muscle strength (kg force)	DMPN Mean (SD)	DFU Mean (SD)	PFA Mean (SD)	TTA Mean (SD)
Hip flexors (affected)	19.93 8.55	21.40 8.94	19.35 7.20	18.43 7.32
Hip flexors (contra-lateral)	18.36 7.95	22.27 8.79	18.90 7.18	16.72 5.68
Hip extensors (affected)	20.74 9.30	23.27 8.83	20.54 9.21	20.63 6.84
Hip extensors (contra-lateral)	20.55 9.86	23.73 8.49	21.35 8.31	18.08 6.45
Hip abductors (affected)	18.57 8.06	18.98 7.85	19.00 7.26	17.48 5.55
Hip abductors (contra-lateral)	18.03 7.81	19.11 7.42	19.00 6.16	16.95 5.36
Hip adductors (affected)	21.62 9.19	22.38 8.48	20.67 7.71	20.33 6.92
Hip adductors (contra-lateral)	19.77 9.06	23.89 9.02	21.96 8.47	18.18 5.86
Knee flexors (affected)	17.38 12.58	19.92 9.03	16.85 6.21	12.58 5.36
Knee flexors (contra-lateral)	17.32 7.75	21.33 10.71	16.35 5.22	17.61 7.02
Knee extensors (affected)	32.54 13.62	33.59 15.86	31.56 11.14	23.20 10.01
Knee extensors (contra-lateral)	30.17 13.03	34.44 13.97	35.89 15.68	26.73 7.80
Ankle plantarflexors (affected)	19.32 8.22	n/a	14.23 8.73	n/a
Ankle plantarflexors (contra-lateral)	18.23 7.77	20.48 8.54	16.062 9.94	13.81 6.58
Ankle dorsiflexors (affected)	14.87 6.49	n/a	14.30 7.36	n/a
Ankle dorsiflexors (contra-lateral)	15.03 5.54	16.13 5.81	14.58 5.83	11.23 2.76

Figures A3.4 to A3.10 demonstrate the mean ROM in the sagittal plane (degrees) at the hip, knee, ankle and 1st MTP joint on the affected and contra-lateral limb respectively.

Figure A3.4: Group means and standard deviations for the hip joint motion in the sagittal plane on the affected limb for all the 4 groups

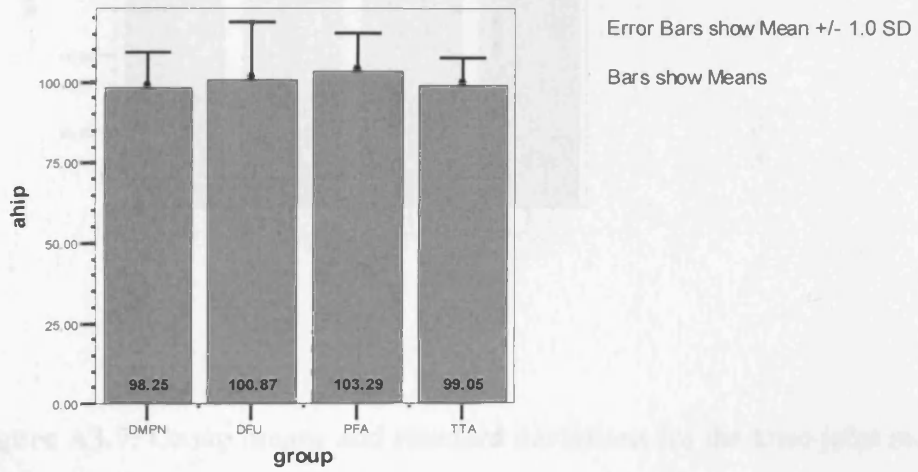


Figure A3.5: Group means and standard deviations for the hip joint motion (degrees) in the sagittal plane on the contra-lateral limb for all the 4 groups

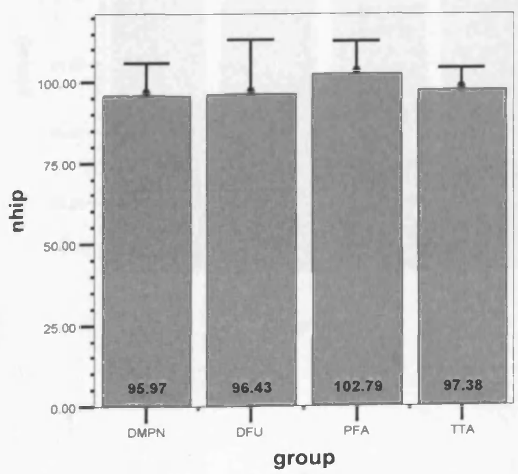


Figure A3.6: Group means and standard deviations for the knee joint motion (degrees) in the sagittal plane on the affected limb for all the 4 groups

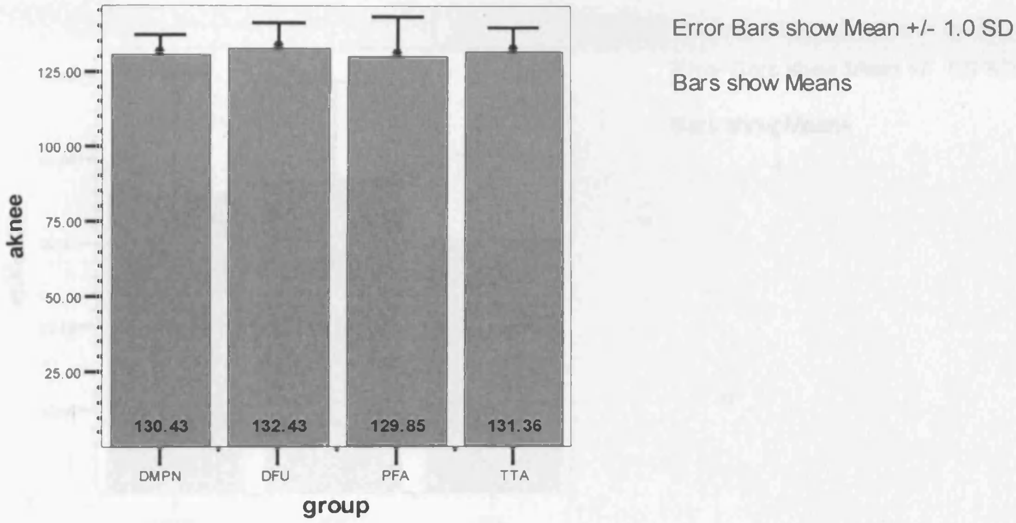


Figure A3.7: Group means and standard deviations for the knee joint motion (degrees) in the sagittal plane on the contra-lateral limb for all the 4 groups

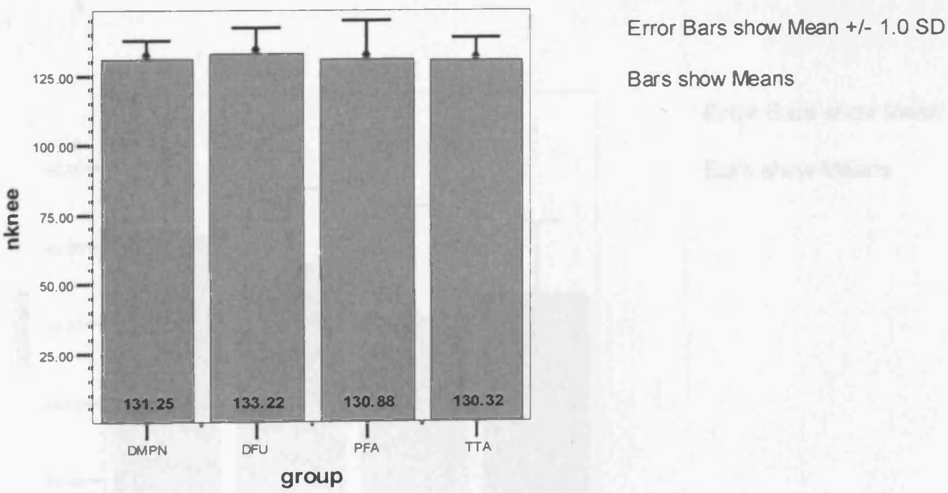


Figure A3.8: Group means and standard deviations for the ankle joint motion (degrees) in the sagittal plane on the affected limb for all the 4 groups

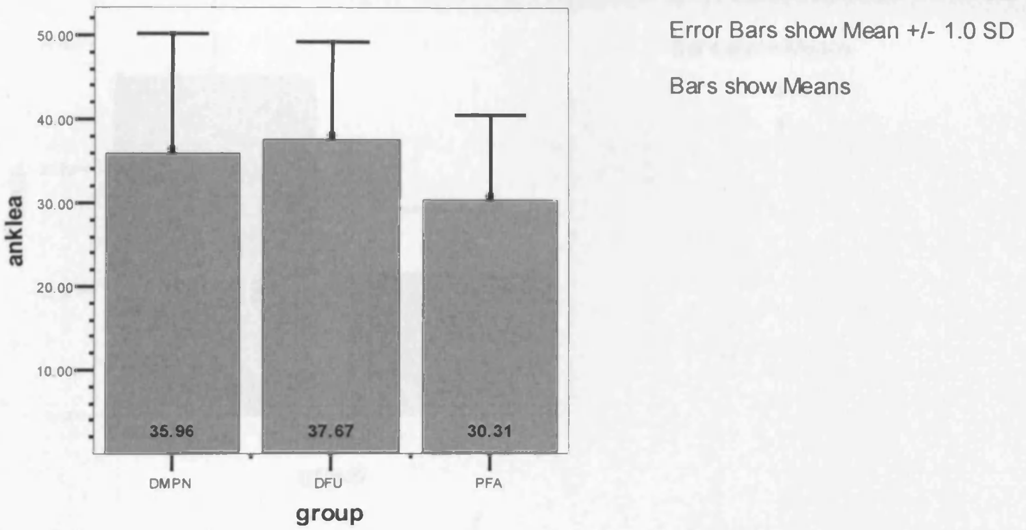


Figure A3.9: Group means and standard deviations for the ankle joint motion (degrees) in the sagittal plane on the contra-lateral limb for all the 4 groups

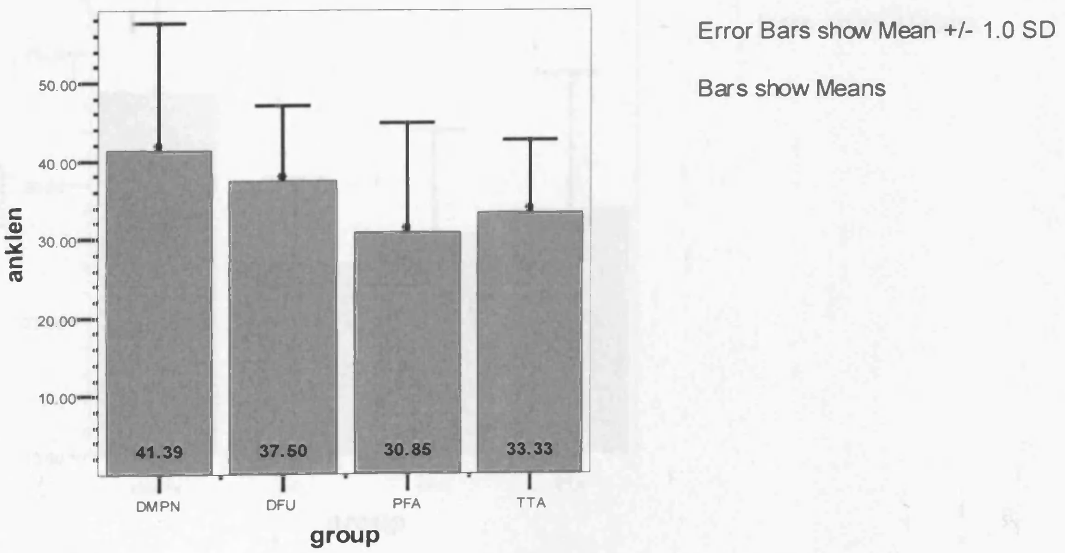


Figure A3.10: Group means and standard deviations for the 1st MTP joint motion (degrees) in the sagittal plane on the affected limb for all the 4 groups

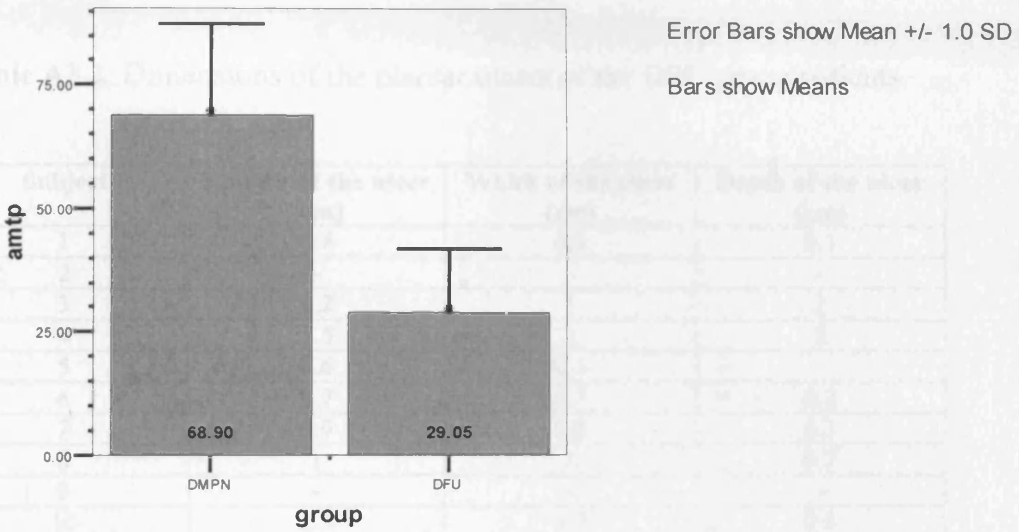


Figure A3.11: Group means and standard deviations for the 1st MTP joint motion (degrees) in the sagittal plane on the contra-lateral limb for all the 4 groups

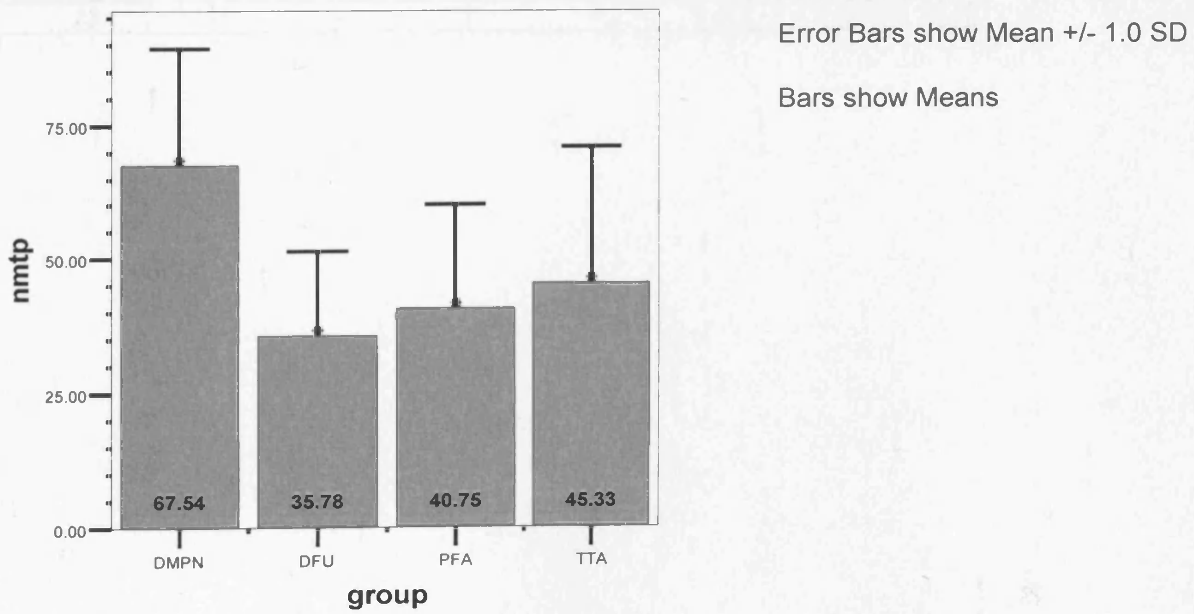


Table A3.2 presents the dimensions of the plantar ulcers of the DFU group patients. The data from 8 patients was missing because of the inability to follow-up with the community podiatrists who had referred the patients for the study.

Table A3.2: Dimensions of the plantar ulcers of the DFU group patients

Subject	Length of the ulcer (cm)	Width of the ulcer (cm)	Depth of the ulcer (cm)
1	0.6	0.4	0.3
2	-	-	-
3	1.2	1	2
4	1.5	1	2
5	0.6	0.5	
6	0.7	0.7	0.2
7	0.9	0.4	0.3
8	1	1	0.7
9	-	-	-
10	2.5	1.7	0.5
11	5.5	2	
12	-	-	-
13	2	0.5	0.5
14	-	-	-
15	1	0.5	0.2
16	1	0.2	0.2
17	1	1	
18	0.5	0.3	0.5
19	-	-	-
20	1	0.5	1.5
21	-	-	-
22	-	-	-
23	-	-	-

Appendix 4

- Instructions to the patients regarding the use of Step Activity Monitor (SAM)

- Rivermead Mobility Index

- SF-36

- Cardiff Wound Impact Scale (Original version)

- Cardiff Wound Impact Scale (The modified version of the original scale was used for the present study. The red lines and the crosses denote the questions, which were deleted for the DMPN, PFA and TTA groups).

STEP WATCH ACTIVITY MONITOR

POINTS TO REMEMBER

1. **Leave it on continuously for ONE week; except during bathing/shower.**
2. **Strap it around the RIGHT ankle joint taking care that the tension is such that it just allows you to pass your finger under the strap, with the monitor resting on the outer aspect of the ankle.**
3. **It is very important to check that the device is placed with the arrow pointing 'UP' which is also indicated by the sticker.**
4. **Watch for swelling around the ankle or the foot.**
5. **In case you notice swelling and have confirmed that the monitor is not strapped too tight; remove the device immediately and contact the Research Centre for Clinical Kinaesiology for further advice.**
6. **Please remember to return the device to the Research Centre after one week.**

Research Centre for Clinical Kinaesiology

Foot/Lower limb function in diabetic neuropathy 2003

NAME:

DATE:

RIVERMEAD MOBILITY INDEX TOPIC AND QUESTION	YES (1)	NO (0)
Turning over in bed. Do you turn over from your back to your side without help?		
Lying to sitting. From lying in bed, do you get up to sit on the edge of the bed on your own?		
Sitting balance. Do you sit on the edge of the bed without holding on for 10 seconds?		
Sitting to standing. Do you stand up from any chair in less than 15 seconds and stand there for 15 seconds, using hands and/or aid if necessary?		
Standing unsupported Observe standing for 10 seconds without any aid		
Transfer. Do you manage to move from a bed to chair and back without any help?		
Walking inside (with an aid if necessary). Do you walk 10 metres, with an aid if necessary, but with no standby help?		
Stairs. Do you manage a flight of stairs without help/		
Walking outside (even ground). Do you walk outside, on pavements without help?		
Walking inside, with no aid. Do you walk 10 metres inside, with no calliper, splint or other aid (including furniture or walls) without help?		
Picking up off the floor. Do you manage to walk 5 metres, pick something up off the floor, and then walk back without help?		
Walking outside (uneven ground). Do you walk over uneven ground (grass, gravel, snow, ice etc.) without help?		
Bathing. Do you get into/out of a bath or shower and wash yourself unsupervised and without help?		
Up and down four steps. Do you manage to go up and down four steps with no rail, but using an aid if necessary?		
Running. Do you run 10 metres without limping in four seconds (fast walking, but no limping is acceptable)		

Issued with step watch number:

Foot/ Lower Limb Function in Diabetic Neuropathy- 2003

THE SHORT FORM 36 HEALTH SURVEY QUESTIONAIRE (SF-36^{TM})

Subject Name: ______________________________ **Group:** ______

Date: ____________________

The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities. If you are unsure about how to answer any question please give the best answer you can and make your own comments if you like. Do not spend too much time in answering as your immediate response is likely to be the most accurate.

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

(Please tick one box)

Excellent ☐

Very Good ☐

Good ☐

Fair ☐

Poor ☐

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

(Please tick one box)

Much better than one year ago ☐

Somewhat better than one year ago ☐

About the same ☐

Somewhat worse now than one year ago ☐

Much worse than one year ago ☐

3. Health and Daily Activities

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

*(Please tick **one** box on each line)*

		Yes, limited a lot	Yes, limited a little	No, Not limited at all
a)	**Vigorous activities** such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
b)	**Moderate activities**, such as moving a table, pushing a vacuum, bowling or playing golf	☐	☐	☐
c)	Lifting or carrying groceries	☐	☐	☐
d)	Climbing **several** flights of stairs	☐	☐	☐
e)	Climbing **one** flight of stairs	☐	☐	☐
f)	Bending, kneeling or stooping	☐	☐	☐
g)	Walking **more than a mile**	☐	☐	☐
h)	Walking **half a mile**	☐	☐	☐
i)	Walking **100 yards**	☐	☐	☐
j)	Bathing and dressing yourself	☐	☐	☐

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

*(Please answer **YES** or **NO** to each question)*

		Yes	No
a)	Cut down on the **amount of time** you spent on work or other activities	☐	☐
b)	**Accomplished less** than you would like	☐	☐
c)	Were limited in the **kind** of work or other activities	☐	☐
d)	Had **difficulty** performing the work or other activities (eg it took more effort)	☐	☐

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

(*Please answer **YES** or **NO** to each question*)

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

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

(*Please tick **one** box*)

Not at all ☐

Slightly ☐

Moderately ☐

Quite a bit ☐

Extremely ☐

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

(*Please tick **one** box*)

None ☐

Very mild ☐

Mild ☐

Moderate ☐

Severe ☐

Very severe ☐

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

*(Please tick **one** box)*

Not at all	☐
A little bit	☐
Moderately	☐
Quite a bit	☐
Extremely	☐

YOUR FEELINGS

9. These questions are about how you feel and how things have been with you **during the past month.** (For each question please indicate the one answer that comes closest to the way you have been feeling).

(Please tick one box on each line)

How much time during **the last month**	**All of the time**	**Most of the time**	**A good bit of the**	**Some of the time**	**A little of the time**	**None of the time**
a) Did you feel full of life?	☐	☐	☐	☐	☐	☐
b) Have you been a very nervous person?	☐	☐	☐	☐	☐	☐
c) Have you felt so down in the dumps that nothing could cheer you up?	☐	☐	☐	☐	☐	☐
d) Have you felt calm and peaceful?	☐	☐	☐	☐	☐	☐
e) Did you have a lot of energy?	☐	☐	☐	☐	☐	☐
f) Have you felt downhearted and low?	☐	☐	☐	☐	☐	☐
g) Did you feel worn out?	☐	☐	☐	☐	☐	☐
h) Have you been a happy person?	☐	☐	☐	☐	☐	☐
i) Did you feel tired?	☐	☐	☐	☐	☐	☐
j) Has your **health limited your social activities** (like visiting friends or close relatives)?	☐	☐	☐	☐	☐	☐

HEALTH IN GENERAL

10. Please choose the answer that best describes how **true** or **false** each of the following statements is for you.

(Please tick **one** box on each line)

	Definitely true	Mostly True	Not sure	Mostly false	Definitely False
a) I seem to get ill more easily than other people	☐	☐	☐	☐	☐
b) I am as healthy as anybody I know	☐	☐	☐	☐	☐
c) I expect my health to get worse	☐	☐	☐	☐	☐
d) My health is excellent	☐	☐	☐	☐	☐

Please note that this section is for the Investigator:

DIMENSION SCORES

Physical function (PF) __________
Role limitation due to physical problems (RP) ________
Role limitation due to emotional problems (RE) ________
Social functioning (SF) ________
Mental health (MH) __________
Energy/vitality (EV) _________
Pain (P) ___________
General health perception (GHP) ______
Change in health (CH) __________

Wound Healing Research Unit

University of Wales College of Medicine

Cardiff Wound Impact Schedule

The following questionnaire is concerned with the effects that your wound has on your daily life. Please answer the questions carefully by placing a tick in the box which most closely reflects how you feel; it should take about ten minutes to complete.

If you are unsure about how to answer a question, please tick the answer which is closest to how you feel. All answers are confidential.

Personal Details

Patient Initials ☐☐☐ **Patient Number** ☐☐☐☐

Date of Birth D D ☐☐ M M ☐☐ Y Y ☐☐

	1st	2nd	3rd	4th	5th
Assessment	☐	☐	☐	☐	☐

Assessment Date ☐☐ ☐☐ ☐☐

Next Assessment Due ☐☐ ☐☐ ☐☐

Wound status Healed ☐ Not Healed ☐

Do you live on your own? Yes ☐ No ☐

How often do you see your family and friends?

Once a day ☐ Once a month ☐

Once a week ☐ Less than once a month ☐

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For Office Use **Total** ☐

Well-being

To what extent do you agree/disagree with the following statements?

	Strongly Disagree	Disagree	Not Sure	Agree	Strongly Agree
I feel anxious about my wound(s)	☐	☐	☐	☐	☐
I feel frustrated at the time it is taking for the wound(s) to heal	☐	☐	☐	☐	☐
I am confident that the wound(s) I have will heal	☐	☐	☐	☐	☐
I worry that I may get another wound in the future	☐	☐	☐	☐	☐
The appearance of the wound site is upsetting	☐	☐	☐	☐	☐
I feel anxious about bumping the wound site	☐	☐	☐	☐	☐
I worry about the impact of the wound(s) on my family/friends	☐	☐	☐	☐	☐

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For Office Use

Total

Physical Symptoms and Daily Living

Have you experienced any of the following during the past week?

	Not at all/ Not applicable	Seldom	Sometimes	Frequently	Always
Disturbed sleep	☐	☐	☐	☐	☐
Difficulty in bathing	☐	☐	☐	☐	☐
Immobility around the home	☐	☐	☐	☐	☐
Immobility outside the home	☐	☐	☐	☐	☐
Leakage from the wound	☐	☐	☐	☐	☐
Pain from the wound site	☐	☐	☐	☐	☐
Discomfort from the bandaging/dressing	☐	☐	☐	☐	☐
Unpleasant odour or smell from the wound	☐	☐	☐	☐	☐
Problems with everyday tasks (eg shopping)	☐	☐	☐	☐	☐
Difficulty in finding appropriate footwear	☐	☐	☐	☐	☐
Problems with the amount of time needed to care for the wound site	☐	☐	☐	☐	☐
Financial difficulties as a result of the wound	☐	☐	☐	☐	☐

For Office Use | **Total** ☐

Physical Symptoms and Daily Living

How stressful has this experience been for you?

	Not at all/ Not applicable	Slightly	Moderately	Quite a bit	Very
Disturbed sleep	☐	☐	☐	☐	☐
Difficulty in bathing	☐	☐	☐	☐	☐
Immobility around the home	☐	☐	☐	☐	☐
Immobility outside the home	☐	☐	☐	☐	☐
Leakage from the wound	☐	☐	☐	☐	☐
Pain from the wound site	☐	☐	☐	☐	☐
Discomfort from the bandaging/dressing	☐	☐	☐	☐	☐
Unpleasant odour or smell from the wound	☐	☐	☐	☐	☐
Problems with everyday tasks (eg shopping)	☐	☐	☐	☐	☐
Difficulty in finding appropriate footwear	☐	☐	☐	☐	☐
Problems with the amount of time needed to care for the wound site	☐	☐	☐	☐	☐
Financial difficulties as a result of the wound	☐	☐	☐	☐	☐

For Office Use — **Total** ☐

Social Life

Have you experienced any of the following during the past week?

	Not at all/ Not applicable	Seldom	Sometimes	Frequently	Always
Difficulty getting out and about	☐	☐	☐	☐	☐
Relying more on others	☐	☐	☐	☐	☐
Your family/friends being over protective	☐	☐	☐	☐	☐
Unable to enjoy your usual social life (eg hobbies)	☐	☐	☐	☐	☐
Limited contact with family/friends	☐	☐	☐	☐	☐
Not going out for fear of bumping your wound site	☐	☐	☐	☐	☐
Wanting to withdraw from people	☐	☐	☐	☐	☐

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For Office Use

Total

Social Life

How stressful has this experience been for you?

	Not at all/ Not applicable	Slightly	Moderately	Quite a bit	Very
Difficulty getting out and about	☐	☐	☐	☐	☐
Relying more on others	☐	☐	☐	☐	☐
Your family/friends being over protective	☐	☐	☐	☐	☐
Unable to enjoy your usual social life (eg hobbies)	☐	☐	☐	☐	☐
Limited contact with family/friends	☐	☐	☐	☐	☐
Not going out for fear of bumping your wound site	☐	☐	☐	☐	☐
Wanting to withdraw from people	☐	☐	☐	☐	☐

For Office Use

Total ☐

Overall Quality of Life

How would you rate your overall quality of life during the past week?

Please circle a number below (Score = number as circled)

How good is your quality of life?

My quality of life is the worst possible	0	1	2	3	4	5	6	7	8	9	10	My quality of life is the best possible

How satisfied are you with your overall quality of life?

Not at all satisfied	0	1	2	3	4	5	6	7	8	9	10	Very satisfied

Overall Comment(s)

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For Office Use

Total

Wound Healing Research Unit

University of Wales College of Medicine

Cardiff Wound Impact Schedule

(MODIFIED)

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The following questionnaire is concerned with the effects that your wound has on your daily life. Please answer the questions carefully by placing a tick in the box which most closely reflects how you feel; it should take about ten minutes to complete.

If you are unsure about how to answer a question, please tick the answer which is closest to how you feel. All answers are confidential.

Personal Details

Patient Initials ☐☐☐ **Patient Number** ☐☐☐☐

Date of Birth D D ☐☐ M M ☐☐ Y Y ☐☐

	1st	2nd	3rd	4th	5th
Assessment	☐	☐	☐	☐	☐

Assessment Date ☐☐ ☐☐ ☐☐

Next Assessment Due ☐☐ ☐☐ ☐☐

Wound status Healed ☐ Not Healed ☐

Do you live on your own? Yes ☐ No ☐

How often do you see your family and friends?

Once a day ☐

Once a week ☐

Once a month ☐

Less than once a month ☐

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For Office Use **Total** ☐

Well-being

To what extent do you agree/disagree with the following statements?

	Strongly Disagree	Disagree	Not Sure	Agree	Strongly Agree
I feel anxious about my wound(s)	☐	☐	☐	☐	☐
I feel frustrated at the time it is taking for the wound(s) to heal	☐	☐	☐	☐	☐
I am confident that the wound(s) I have will heal	☐	☐	☐	☐	☐
I worry that I may get another wound in the future	☐	☐	☐	☐	☐
The appearance of the wound site is upsetting	☐	☐	☐	☐	☐
I feel anxious about bumping the wound site	☐	☐	☐	☐	☐
I worry about the impact of the wound(s) on my family/friends	☐	☐	☐	☐	☐

For Office Use **Total** ☐

Physical Symptoms and Daily Living

Have you experienced any of the following during the past week?

	Not at all/ Not applicable	Seldom	Sometimes	Frequently	Always
Disturbed sleep	☐	☐	☐	☐	☐
Difficulty in bathing	☐	☐	☐	☐	☐
Immobility around the home	☐	☐	☐	☐	☐
Immobility outside the home	☐	☐	☐	☐	☐
Leakage from the wound X	☐	☐	☐	☐	☐
Pain from the wound site X	☐	☐	☐	☐	☐
Discomfort from the bandaging/dressing X	☐	☐	☐	☐	☐
Unpleasant odour or smell from the wound X	☐	☐	☐	☐	☐
Problems with everyday tasks (eg shopping)	☐	☐	☐	☐	☐
Difficulty in finding appropriate footwear	☐	☐	☐	☐	☐
Problems with the amount of time needed to care for the wound site X	☐	☐	☐	☐	☐
Financial difficulties as a result of the wound X	☐	☐	☐	☐	☐

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For Office Use

Total

Physical Symptoms and Daily Living

How stressful has this experience been for you?

	Not at all/ Not applicable	Slightly	Moderately	Quite a bit	Very
Disturbed sleep	☐	☐	☐	☐	☐
Difficulty in bathing	☐	☐	☐	☐	☐
Immobility around the home	☐	☐	☐	☐	☐
Immobility outside the home	☐	☐	☐	☐	☐
Leakage from the wound X	☐	☐	☐	☐	☐
Pain from the wound site X	☐	☐	☐	☐	☐
Discomfort from the bandaging/dressing X	☐	☐	☐	☐	☐
Unpleasant odour or smell from the wound X	☐	☐	☐	☐	☐
Problems with everyday tasks (eg shopping)	☐	☐	☐	☐	☐
Difficulty in finding appropriate footwear	☐	☐	☐	☐	☐
Problems with the amount of time needed to care for the wound site X	☐	☐	☐	☐	☐
Financial difficulties as a result of the wound X	☐	☐	☐	☐	☐

For Office Use

Total

Social Life

Have you experienced any of the following during the past week?

	Not at all/ Not applicable	Seldom	Sometimes	Frequently	Always
Difficulty getting out and about	☐	☐	☐	☐	☐
Relying more on others	☐	☐	☐	☐	☐
Your family/friends being over protective	☐	☐	☐	☐	☐
Unable to enjoy your usual social life (eg hobbies)	☐	☐	☐	☐	☐
Limited contact with family/friends	☐	☐	☐	☐	☐
Not going out for fear of bumping your wound site X	☐	☐	☐	☐	☐
Wanting to withdraw from people	☐	☐	☐	☐	☐

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For Office Use

Total

Social Life

How stressful has this experience been for you?

	Not at all/ Not applicable	Slightly	Moderately	Quite a bit	Very
Difficulty getting out and about	☐	☐	☐	☐	☐
Relying more on others	☐	☐	☐	☐	☐
Your family/friends being over protective	☐	☐	☐	☐	☐
Unable to enjoy your usual social life (eg hobbies)	☐	☐	☐	☐	☐
Limited contact with family/friends	☐	☐	☐	☐	☐
Not going out for fear of bumping your wound site X	☐	☐	☐	☐	☐
Wanting to withdraw from people	☐	☐	☐	☐	☐

For Office Use **Total**

Overall Quality of Life

How would you rate your overall quality of life during the past week?

Please circle a number below (Score = number as circled)

How good is your quality of life?

My quality of life is the worst possible	0	1	2	3	4	5	6	7	8	9	10	My quality of life is the best possible

How satisfied are you with your overall quality of life?

Not at all satisfied	0	1	2	3	4	5	6	7	8	9	10	Very satisfied

Overall Comment(s)

c:\pp\other\qolq2/98/2

For Office Use

Total

List of manuscripts related to the present study

Published articles:

1. Risk of plantar ulceration in diabetic patients with single-leg amputation.
Kanade RV, van Deursen RWM, Price P, et al.Clinical Biomechanics 21 (3): 306-313 MAR 2006.

2. Walking performance in people with diabetic neuropathy: benefits and threats.
R. V. Kanade, R. W. M. van Deursen, K. Harding and P. Price. Diabetologia 49 (8) August 2006 (Published online: 7 June 2006).

3. Difficulties in recruiting subjects with partial foot amputations for kinesiological research.
R. V. Kanade, R. W. M. van Deursen, K. Harding and P. Price The Foot (2006), doi:10.1016/j.foot.2006.08.002

Submitted:

1. Research Article: Re-amputation rate in the diabetic patients referred to the artificial limb and appliance centres in South Wales, UK.
RV Kanade, RWM van Deursen, Jo Burton, Vanessa Davies, Patricia Price
International Wound Journal

Abstracts:

1. Daily walking activity following partial foot amputations in diabetic people
Rajani V Kanade; Dr. Robert van Deursen; Prof. Patricia Price; Prof. Keith Harding
Research Centre for Clinical Kinaesiology, Physiotherapy & Wound Healing Research Unit. Research Day, Cardiff University 2005.

2. Daily walking activity following partial foot amputations in diabetic People.
Kanade RV, Price PE, Harding KG, van Deursen RWM
Research Centre for Clinical Kinaesiology, Wound Healing Research Unit, Cardiff University, Wales, UK. O25: DFSG 2005. Kassandra, Chalkidiki, Greece 7-10 September.

3. Daily Walking Activity In The Presence Of Diabetic Foot Ulcers.
van Deursen RWM, Price PE, Harding KG, Kanade RV
Research Centre for Clinical Kinaesiology, 2Wound Healing Research Unit, Cardiff University, Wales, UK. O33: DFSG 2005. Kassandra, Chalkidiki, Greece. 7-10 September.

4. Functional outcome in people with trans-tibial amputations related to Diabetes.
Kanade RV, Price PE, Harding KG, van Deursen RWM
Research Centre for Clinical Kinaesiology, Wound Healing Research Unit, University of Wales College of Medicine, Cardiff, UK. O24: DFSG 2004. Regensburg, Germany. 2-5 September.

5. Risk of plantar ulceration to the surviving foot in the patients with diabetic neuropathy following trans-tibial amputation.
Kanade RV, Price PE, Harding KG, van Deursen RWM
Research Centre for Clinical Kinaesiology, 2Wound Healing Research Unit, Cardiff University, Wales, UK. ESM 2004. Leeds, UK. 29th July-1st Aug

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Risk of plantar ulceration in diabetic patients with single-leg amputation

R.V. Kanade [a], R.W.M. van Deursen [a,*], Patricia Price [b], Keith Harding [b]

[a] *Research Centre for Clinical Kinaesiology, Department of Physiotherapy, School of Healthcare Studies, Cardiff University, Ty Dewi Sant, Health Park, Cardiff CF14 4XN, United Kingdom*
[b] *Wound Healing Research Unit, School of Medicine, Cardiff University, Cardiff CF14 4UJ, United Kingdom*

Received 17 June 2005; accepted 15 October 2005

Abstract

Background. There is a disconcerting rate of bilateral limb loss in patients with diabetes. Therefore, this study aimed to explore plantar loading of the surviving foot following unilateral trans-tibial amputation within a wider context of daily walking activity to investigate the precise risk to the surviving limb.

Methods. Twenty-one subjects with diabetic neuropathy and trans-tibial amputation were matched for weight; height; age and gender with 21 control subjects with diabetic neuropathy without history of plantar ulceration. Gait parameters, in-shoe plantar pressure distribution and daily walking (using the step activity monitor) were recorded. *Student's t*-tests were used to compare groups (α-level: 0.05).

Findings. The trans-tibial amputations group walked almost 30% slower compared to controls ($P < 0.01$), with reduced cadence ($P < 0.01$), and shorter strides ($P < 0.01$). Despite walking slower, the surviving foot showed higher mean peak plantar pressures in the trans-tibial amputations group over the heel ($P < 0.001$) however there was no significant difference over the I–II and lateral III–IV–V metatarso-phalangeal regions. Pressure time integral was higher over the heel ($P < 0.00$), I–II ($P < 0.01$) and III–IV–V metatarso-phalangeal ($P < 0.05$) in the trans-tibial amputations group. The amputee group walked less steps per day ($P < 0.01$).

Interpretation. Adaptations in gait and level of walking activity affect plantar pressure distribution and ultimately the risk of ulceration to the surviving foot. Therefore rehabilitation measures should consider implications for plantar loading and the potential risk of ulceration to the surviving foot.

Keywords: Surviving foot; Plantar ulceration; Diabetic neuropathy; Trans-tibial amputation; Physiotherapy

1. Introduction

Individuals with diabetes mellitus (DM) have a fifteen fold higher rate of lower extremity amputation than those without diabetes (Most and Sinnock, 1983). 6–30% of the amputee population undergo contra-lateral lower extremity amputation within 1–3 years of their initial amputation (Reiber, 1996) and a patient with DM with single limb amputation has a 50% (Hoar, 1962) to 66% (Goldner, 1960) incidence of contra-lateral lower extremity amputation within 5 years. Despite the disconcerting rate of contra-lateral limb loss, this problem appears to be addressed inadequately by the rehabilitation care systems owing to the limited evidence in this area (Broomhead et al., 2003). Data from objective gait analysis of the contra-lateral limb following unilateral lower extremity amputation appear to confirm the clinical impression that unilateral amputees are more stable and accept increased pressure on their remaining contralateral "limb-at-risk" during walking compared to the

* Corresponding author.
E-mail address: vandeursenr@cardiff.ac.uk (R.W.M. van Deursen).

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amputated side (Pinzur et al., 1991). However, the exact relationship between the contributing factors related to walking leading to further plantar tissue injury remains unclear.

There has been some work completed on the loading of the contra-lateral limb in below-knee amputees. Pinzur et al. (1991) studied the impact of trans-tibial amputations (TTA) on the loading of contra-lateral foot in patients with peripheral vascular insufficiency and concluded that risk of contra-lateral LEA is related to systemic peripheral vascular insufficiency or local factors and not increased loading of the remaining contra-lateral "limb-at-risk". Powers et al. (1994) and Snyder et al. (1995) investigated the influence of prosthetic foot design on the loading of the in-tact limb in cases of traumatic and dysvascular TTA, respectively. They recorded greater vertical loading force to the sound limb and concluded that prosthetic foot design can have an effect on the magnitude of vertical forces experienced by the limb. Despite the high incidence of contra-lateral lower extremity amputation in diabetic patients, to our knowledge only two studies have directly addressed the issue of plantar loading of the surviving foot in this patient population. Veves et al. (1992) studied peak plantar pressures over the surviving foot of subjects with unilateral major lower extremity amputation with DM compared to subjects with lower extremity amputation without DM; subjects with diabetic peripheral neuropathy (DMPN) and non-diabetic control subjects. They demonstrated higher foot pressures over the remaining foot of the diabetic amputees and concluded that amputation itself does not increase pressures under the remaining foot but attributed the increased levels to DMPN. However, in the light of evidence in the literature on the relationship between gait velocity and plantar pressures their report is not very clear regarding the consideration of walking speed in the interpretation of plantar pressure distribution. Peak pressures are known to rise with increasing gait velocity (Burnfield et al., 2004). Hayden et al. (2000) studied the effect of various prosthetic feet on the pattern of plantar pressure distribution on the sound limb of unilateral trans-tibial diabetic amputees during walking. They concluded that the type of prosthetic foot used did not significantly affect peak plantar pressures on the surviving foot, except the heel region.

The influence of level of weight bearing activity on the mechanical trauma accumulated by plantar tissues among individuals with diabetes has been identified (Cavanagh et al., 1996). However, the impact of daily weight-bearing activity on the potential risk of plantar ulceration resulting from cumulative plantar stress to the surviving foot has not been studied. Maluf and Mueller (2003) have studied daily weight-bearing activity and cumulative plantar tissue stress in subjects with DMPN. Their findings suggest that plantar tissues may be more susceptible to injury at relatively low levels of cumulative stress following an initial episode of skin breakdown. However, no studies to our knowledge have investigated the impact of daily walking activity on the surviving foot of diabetic people following unilateral amputations though walking is a commonly encountered essential weight bearing activity of daily life.

Therefore though the literature has addressed the issue of weight bearing on the contra-lateral foot following unilateral lower extremity amputations, further investigation to explore plantar loading of the surviving foot within a wider context of daily walking activity is lacking. Walking is an essential weight-bearing activity of daily life. Considering the disconcerting rate of contra-lateral limb amputations in diabetic people it is essential to explore the contribution of daily walking activity to the plantar loading of the contra-lateral foot. The authors believe that this might help to guide the focus of rehabilitation services in the direction of safeguarding the surviving foot. Our objectives were to compare the differences in the gait characteristics and daily walking activity and their respective influence on plantar loading between the subjects with DMPN and unilateral TTA and subjects with DMPN without history of plantar ulceration.

2. Methods

2.1. Subjects

Following written, informed consent, 21 subjects with DMPN and unilateral TTA were matched on marginal distributions of weight; height; age and gender with 21 control subjects with DMPN without history of plantar ulceration. Semmes Weinstein monofilaments were used to confirm the neuropathy status (Kumar et al., 1991). Neuropathy was considered present if the 5.07 (10 g) Semmes Weinstein monofilament (loss of protective sensation) was not perceived in at least one of these four plantar areas tested (Hallux; Ist metatarsal head; Vth metatarsal head and heel). Five to ten trials were performed at each site (Diamond et al., 1989) and the subject needed to perceive 80% of the trials to be graded as the sensation present over that site. The site was scored 1 in case of presence of sensation and 0 in case of absence of the sensation. The sum of the scores over the four sites was used to present the final sensory score over the entire foot.

2.2. Selection criteria

Subjects within the age range of 40–75 yrs, living independently in the community with visual acuity of minimum 20/40 in the better eye (pre-requisite to obtain a driving license) and an ability to communicate without support were included. All the participants were active walkers with or without a walking aid and always used their artificial limb for walking. However, no walking aids were used during the testing procedures. All the subjects with TTA were at least six months post-amputation following rehabilitation at the time of discharge from Artificial Limb and Appliance Centers (South Wales). None of the subjects from either group showed any clinical evidence of current plantar ulceration. One subject from the study group had an amputation of the fourth digit of the surviving foot prior to the study. This subject was included in the study for two reasons: the biomechanical changes associated with a lesser digit amputation with preservation of the metatarsal head are not large (Greteman and Dale, 1990) and the data confirmed this subject was not an outlier.

2.3. Exclusion criteria

Patients with bilateral LEA; gross neurological and musculo-skeletal impairments or painful form of DMPN were excluded from the study. Subjects taking medication with known effects on the central nervous system; known dependence on alcohol and or drugs were also excluded. Subjects presenting with acute symptoms of nephropathy or cardio-vascular complications resulting from DM or any other major chronic illnesses were excluded.

2.4. Instrumentation and procedure

Plantar pressure distribution was measured using the Pedar in-shoe pressure measurement system (novel, Gmbh, Munich, Germany) at a sampling rate of 50 Hz. Two millimeters thick insoles available in different standard and wide sizes were used. The insoles were calibrated using the standard calibration device with homogenous air pressure ranging from 4 to 60 N/cm^2. Zero measurement was performed before starting the measurement. Each subject walked a distance of 12 m at their self-selected pace. Three trials were recorded for each subject (Mcpoil et al., 1999) as they walked on level ground between two parallel calibration sticks placed 1 m apart whilst being recorded using a digital camcorder with a sampling rate of 25 Hz. Spatial and temporal parameters of gait were determined using a purpose-written programme in Matlab 6.5 (Van Deursen et al., 2001).

Stepwatch Activity Monitors (SAM; Prosthetics Research Study, Seattle, WA, USA) were used to record the performance of daily walking activity (Shepherd et al., 1999). The SAM is known to be a reliable and valid tool for the measurement and recording of walking activity (Hartsell et al., 2002). The accelerometer-based device measuring $680 \times 50 \times 20$ mm was strapped around the subject's right leg laterally above the ankle joint (Fig. 1) and the monitor's sensitivity and sampling rate was optimized according to the height and gait

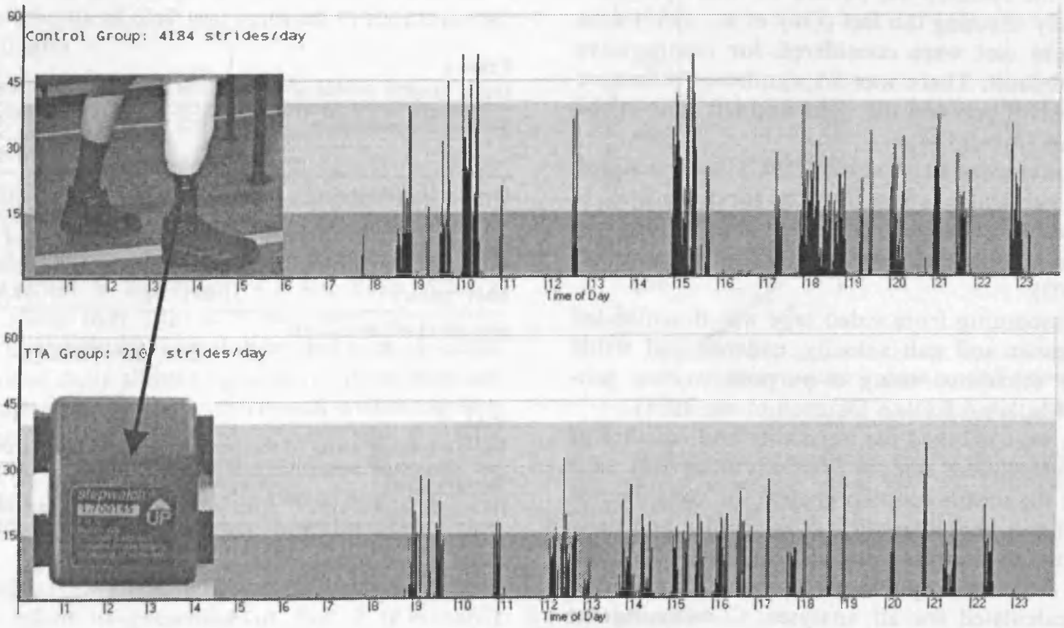

Fig. 1. SAM strapped to the patient's right leg (prosthetic limb as seen in this picture). Typical 24 h physical activity pattern (strides recorded every minute) of a subject from the control group (top graph: 4184 strides/24 h) and the TTA group (bottom graph: 2107 strides/24 h). The dark grey band indicates low levels of activity.

characteristics of each individual subject. In case of subjects with right TTA the device was worn on the prosthetic limb. Subjects were instructed to wear SAM continuously for eight consecutive days, except when bathing, showering or swimming. The number of strides every 1 min interval were recorded for a continuous 24 h over seven consecutive days.

2.5. Data processing and analysis

Plantar pressure data were analysed using novel standard software version 10.33. Five mid-gait steps on each foot, right and left were selected for further analysis. The step analysis program was used to analyse the parameters of maximum peak pressure (MPP), pressure–time integral (PTI) and average velocity of centre of pressure (CoP) line. MPP reflects the absolute peak pressure. Since tissue vulnerability is a factor of both time and pressure (Brand, 1983), pressure–time integral (PTI) was studied as the area under the peak pressure–time curve. Cornwall and Mcpoil (2000) have reported the average velocity of CoP as a reliable measurement tool in gait assessment. The average velocity of CoP line was studied to investigate the plantar loading across the stance phase of the gait cycle (Hayes et al., 1998). Individual masks were created for each subject subdividing the foot into six regions namely, the heel, midfoot; Ist and IInd MTP (*metatarso-phalangeal region*); IIIrd, IVth and Vth MTP; hallux and all the toes. The plantar pressure data obtained from the surviving foot were compared to data from right foot of the control group. Considering the symmetrical pattern of distal polyneuropathy chiefly affecting the feet (Guy et al., 1985) data from the right feet were considered for comparative analysis by default. There was no significant difference in the total MPP between the right and left foot in the control group ($P = 0.134$).

Daily plantar cumulative stress (DPCS) was analysed to study the cumulative stress over the surviving foot. It was computed as a product of average daily strides and PTI over the total surface area of the foot (Maluf and Mueller, 2003).

The gait recording from video tape was downloaded to the computer and gait velocity, cadence and stride length were calculated using a purpose written programme in Matlab 6.5 (Van Deursen et al., 2001).

The data were checked for normality and equality of variance. Independent sample *Student's t*-test was used to compare the means for two groups for the outcome measures of gait characteristics; daily strides and daily plantar cumulative stress with critical level of significance ($P \leq 0.05$). Ninety-five percent confidence intervals were calculated for all analyses. Considering the influence of gait velocity on peak pressures (Burnfield et al., 2004). Analysis of co-variance was used to compare the means of the parameters of pressure distribution with gait velocity as the covariate since the subjects had walked at self-selected speeds. Pearson's correlation coefficient (r) was used to examine the relationship between daily plantar cumulative stress and daily walking activity.

3. Results

The subject characteristics of both the groups are presented in Table 1. The sensory score from the two groups is presented in Table 2. All subjects had loss of protective sensation over at least one plantar area tested. A large majority in both groups had loss of protective sensation in more than one area (TTA group: 16/21; controls: 19/21). Exploration of a relationship between the sensory score (0–4) and peak pressures did not reveal an association between these variables in these groups.

3.1. Gait characteristics and pressure distribution

The amputee group walked with significantly lesser cadence ($P < 0.01$); slower gait velocity ($P < 0.001$) and shorter strides ($P < 0.001$) as presented in Table 3. Despite walking slower, the surviving foot showed significantly higher pressure over the heel ($P < 0.001$) and marginally higher mean MPP values over the entire foot ($P = 0.129$); I–II MTP ($P = 0.231$) and III–IV–V MTP ($P = 0.799$) though these differences were not significant as demonstrated in Table 4. The PTI values over the entire foot ($P < 0.001$) and regions of heel ($P < 0.001$), I–II MTP ($P < 0.01$) and III–IV–V MTP ($P < 0.05$) were

Table 1
Demo graphic profile of the subjects from both the groups

Subject characteristics	Control ($n = 21$)	TTA ($n = 21$)
	Mean (SD)	Mean (SD)
Gender (female/male)	3/18	2/19
Age (yrs)	63.81 (5.71)	62.9 (6.23)
Height (cm)	174.35 (7.73)	174.29 (5.42)
Mass (kg)	94.47 (11.84)	95.49 (15.01)
BMI (kg/m^2)	31.10 (3.6)	31.37 (4.30)

SD: standard deviation.

Table 2
Plantar sensory score of the subjects from both the groups

Sensory score (min = 0; max = 4)	Control (no. of subjects)	TTA (no. of subjects)
0	4	14
1	4	1
2	11	1
3	2	5
4	0	0

A score of 0 indicates that the 10 g monofilament was not perceived in any plantar area.

Table 3
Gait characteristics, daily walking activity and daily plantar cumulative stress of the subjects from both the groups

Walking activity	Control group	TTA group	Significance
	Mean (SD)	Mean (SD)	
Cadence (steps/min)	100 (10)	90 (10)	$P < 0.01^*$
Gait velocity (m/s)	1.08 (0.20)	0.76 (0.14)	$P < 0.001^*$
Stride length (m)	1.29 (0.18)	1.01 (0.12)	$P < 0.001^*$
Daily strides (strides/day)	4114 (1932)	1941 (1084)	$P < 0.001^*$
DPCS	505.71 (235.67)	355.60 (211.05)	$P < 0.05^*$

SD: standard deviation.
DPCS: daily plantar cumulative stress (MPa/day).
* Significant ($P < 0.05$).

Table 4
Plantar pressure distribution of the subjects from both the groups compared using ANCOVA with gait velocity as the co-variate

Plantar pressure distribution	Control group	TTA group	Significance
	Mean (SD)	Mean (SD)	
MPP total foot	321.74 (60.39)	347.73 (78.37)	$P = 0.129$
MPP heel	241.28 (40.28)	252.37 (45.77)	$P < 0.01^*$
MPP I II MT	299.17 (73.29)	316.25 (91.84)	$P = 0.231$
MPP III IV V MT	268.64 (81.39)	248.48 (77.57)	$P = 0.799$
PTI total foot	125.56 (29.71)	180.62 (40.47)	$P < 0.01^*$
PTI heel	62.37 (13.94)	101.95 (25.81)	$P < 0.01^*$
PTI I II MT	75.46 (24.90)	111.52 (43.91)	$P < 0.01^*$
PTI III IV V MT	73.28 (28.81)	95.88 (38.89)	$P < 0.05^*$
Avg vel COP	0.34 (0.09)	0.26 (0.04)	$P < 0.01^*$

SD: standard deviation.
MPP, maximum peak pressure (kPa); PTI, pressure time integral (kPa s); I II MT, first and second metatarsal region; III IV V MT, third, fourth and fifth metatarsal region; avg vel COP, average velocity of centre of pressure (m/s).
* Significant ($P < 0.05$).

significantly higher in TTA group compared to controls. The average velocity of CoP was reduced in the amputee group ($P < 0.001$).

3.2. Daily walking activity and daily plantar cumulative stress

The amputee group walked fewer steps per day compared to the controls resulting in a significantly lower daily average stride count ($P < 0.001$). Reduced walking activity did reflect in significantly lower daily plantar cumulative stress over the surviving foot ($P < 0.05$). We found a significant correlation between average daily strides and daily plantar cumulative stress between the two groups ($r = 0.867$; $P < 0.01$) and within the two groups, respectively (Control group: $r = 0.906$; $P < 0.01$ and TTA group: $r = 0.881$; $P < 0.01$). Since the correlations were not different within the two groups the data from the two groups were merged together for further exploration. A positive linear relationship was found between Daily Plantar cumulative stress and average daily stride count as presented in Fig. 2 ($r = 0.867$; $P < 0.001$). However, PTI did not significantly relate to daily plantar cumulative stress ($r = -0.018$; $P = 0.910$).

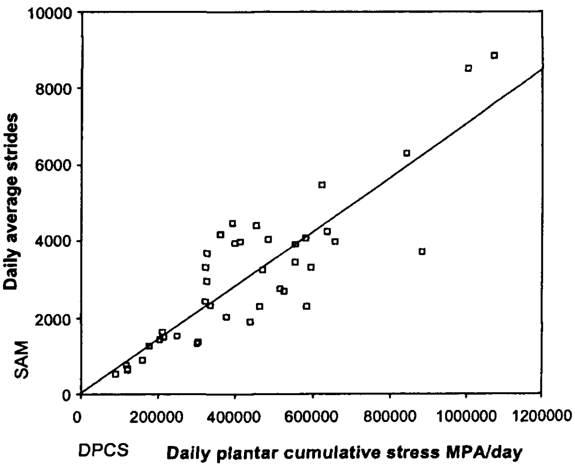

Fig. 2. Relationship between daily walking performance (SAM) and daily plantar cumulative stress (DPCS). Correlation coefficient between two variables is 0.867 ($P < 0.001$).

4. Discussion

The findings from this study demonstrate that unilateral TTA results in adaptations in the pattern of gait and daily walking activity. The amputee group walked slower, with lesser cadence and shorter strides. Menz et al. (2004) and Courtemanche et al. (1996) have reported a conservative gait pattern in people with DMPN without amputations compared to healthy matched subjects (without diabetes). In our study, the pronounced conservative gait pattern in the TTA group may be attributed to complete sensory loss from the prosthetic limb and impaired sensory feedback from the surviving foot.

Although peripheral neuropathy and higher peak pressures are associated with plantar ulceration in the diabetic population (Frykberg et al., 1998) our results did not demonstrate any association between neuropathy score and peak pressures despite the decreased sensory score of the TTA group compared to the controls. However the significant difference in gait velocity between the two groups was considered since peak pressures are known to rise with increasing gait velocity (Burnfield et al., 2004). With this conjecture, the pressures should be lower with reduced walking speed in the TTA group. But we did not control the speed of walking as this might have influenced the natural gait pattern of the subjects consequently affecting the pressure distribution. Therefore reduction in the gait velocity was accommodated in the statistical analyses to avoid any biased interpretation of the peak pressures. Despite walking 30% slower, the surviving foot presented with significantly higher peak pressures over the heel region. However the remaining areas of the foot demonstrated marginally higher mean MPP compared to the controls though the difference was not statistically significant. Therefore this deceptive MPP picture needs to be interpreted with caution as it actually underestimates the underlying risk of plantar injury to the surviving foot.

Though the peak pressures did not vary significantly between the two groups over the entire foot surface area, significantly higher PTI and decreased average velocity of CoP in the amputee group indicate prolonged load bearing on the surviving foot. This would presumably be related to the slower gait velocity. The relevance of the relationship between pressure time and skin breakdown has previously been highlighted (Sanders et al., 1995). The total plantar surface area of the surviving foot in the TTA group showed significantly higher total PTI values and higher regional PTI values over the heel, I–II MTP and III–IV–V MTP areas. Increased stress at the metatarsal heads is a large contributory factor for occurrence of ulceration compared to other regions of the foot (Sauseng et al., 1999).

Limited joint mobility is also known to be a factor in the causation of plantar ulceration in the neuropathic foot (Fernando et al., 1991). Additionally, micro vascular changes are known to contribute to the aetiology of plantar injury in addition to increased mechanical stress in the presence of diabetic neuropathy (Cavanagh et al., 1996). Normally, a pressure of 100 mmHg (equivalent to 13.3 kPa) occludes the capillary blood flow (Cavanagh et al., 1996). Plantar pressures during both standing and walking on normal foot are easily sufficient to occlude capillary blood flow (e.g. plantar pressures in the metatarsal head region are 400 kPa) (Rosenbaum et al., 1994). In the case of neuropathic patients a number of local reflexes, including the hyperaemic response are modified (Tooke et al., 1987) and this can influence the recovery of vascularity of plantar tissues. It is also suggested that capillary fragility may be greater in people with diabetes (Tooke et al., 1987). In the light of all these factors, prolonged weight-bearing can potentially contribute to increase the vulnerability of the surviving foot to plantar injury.

In addition, it is important to consider the effect of cumulative daily walking activity over a day on the cumulative plantar stress. The TTA group walked less than half the volume of steps daily compared to the control group. This reduced daily walking activity resulted in a lower level of DPCS in the TTA group. Though it has been established that moderate repetitive stress causes ulceration (Bauman and Brand, 1963); based on the recently emerging association of decreased DPCS with the risk of plantar injury (Maluf and Mueller, 2003) the surviving foot following TTA presents with the underlying risk of plantar injury. However, since we do not have evidence to suggest a critical level of plantar pressure to identify patients at risk for neuropathic foot ulceration (Armstrong et al., 1998) it is hard to prescribe an optimal, safe level of daily walking activity.

Consequently prophylactic care of the surviving foot following TTA gains a pivotal role in the rehabilitation of diabetic amputees. The focus of amputee rehabilitation appears to be guided by prosthetic limb training with little attention to the surviving foot (Leonard et al., 2004). Although we acknowledge that it is essential to restore the ambulant mobility of the patient following amputation, it is necessary to emphasize the importance of implications for plantar loading in the light of potential risk of plantar ulceration. Despite walking slower, the mean values of MPP are marginally higher over the surviving foot. Though the peak plantar pressures over the remaining areas of the surviving foot other than the heel were not significantly higher, they remain clinically important. Greater emphasis on weight-bearing activities or increasing the speed and volume of walking in the diabetic amputee population could consequently result in higher peak pressures making the surviving foot more vulnerable to damage. Therefore, adequate protection of the surviving foot during essential weight-bearing activities gains paramount importance in rehabilitation.

5. Conclusions

We conclude that adaptations in gait and level of walking activity affect the plantar pressure distribution and ultimately the potential risk of ulceration to the surviving foot. Prolonged plantar load-bearing indicated by significantly higher PTI and slower average velocity of CoP with decreased plantar cumulative stress exacerbates the potential risk of plantar injury. Though the peak plantar pressures over the remaining areas of the surviving foot other than the heel were not significantly higher, they remain clinically important. Efforts to increase the speed and volume of walking might pose the surviving foot to a greater risk of injury. Therefore rehabilitation measures generally aimed to increase weight-bearing and ambulant mobility should consider implications for plantar loading and risk of ulceration to the surviving foot following trans-tibial amputations in the presence of diabetic neuropathy with adequate protection of the surviving foot as the pivotal point of rehabilitation care.

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ARTICLE

Walking performance in people with diabetic neuropathy: benefits and threats

R. V. Kanade · R. W. M. van Deursen · K. Harding · P. Price

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Abstract
Aims/hypothesis Walking is recommended as an adjunct therapy to diet and medication in diabetic patients, with the aim of improving physical fitness, glycaemic control and body weight reduction. Therefore we evaluated walking activity on the basis of capacity, performance and potential risk of plantar injury in the diabetic population before it can be prescribed safely.
Subjects, materials and methods Twenty-three subjects with diabetic neuropathy (DMPN) were compared with 23 patients with current diabetic foot ulcers, 16 patients with partial foot amputations and 22 patients with trans-tibial amputations. The capacity for walking was measured using a total heart beat index (THBI). Gait velocity and average daily strides were measured to assess the performance of walking, and its impact on weight-bearing was studied using maximum peak pressure.
Results THBI increased ($p<0.01$) and gait velocity and daily stride count fell ($p<0.001$ for both) with progression of foot complications. The maximum peak pressures over the affected foot of patients with diabetic foot ulcers ($p<0.05$) and partial foot amputations ($p<0.01$) were higher than in the group with DMPN. On the contralateral side, the diabetic foot ulcer group showed higher maximum peak pressure over the total foot ($p<0.05$), and patients with partial foot amputations ($p<0.01$) and trans-tibial amputations ($p<0.05$) showed higher maximum peak pressure over the heel.
Conclusions/interpretation Walking capacity and performance decrease with progression of foot complications. Although walking is recommended to improve fitness, it cannot be prescribed in isolation, considering the increased risk of plantar injury. For essential walking we therefore recommend the use of protective footwear. Walking exercise should be supplemented by partial or non-weight-bearing exercises to improve physical fitness in diabetic populations.

Keywords Diabetic foot ulcers · Diabetic neuropathy · Partial foot amputations · Peak pressures · Physical fitness · Trans-tibial amputation · Walking

Abbreviations

DFU	diabetic foot ulcer
DMPN	diabetic neuropathy
H-R QOL	health-related quality of life
LEA	lower extremity amputation
MPP	maximum peak pressure
MT	metatarsal
PFA	partial foot amputation
SAM	step activity monitor
THBI	total heart beat index
TTA	trans-tibial amputation

Introduction

Walking is a common activity of daily life. It is recommended as an adjunct therapy to dietary treatment in obese

R. V. Kanade · R. W. van Deursen (✉)
Research Centre for Clinical Kinaesiology,
Department of Physiotherapy, Cardiff University,
Ty Dewi Sant, Heath Park,
Cardiff CF14 4XN, UK
e-mail: vandeursenr@cardiff.ac.uk

K. Harding · P. Price
Wound Healing Research Unit, School of Medicine,
Cardiff University,
Cardiff, UK

type 2 diabetic patients, not only for body weight reduction, but also for improvement of insulin sensitivity [1]. Ten thousand steps per day are reported to result in improved glucose tolerance and a reduction in systolic and diastolic blood pressure in overweight women at risk of type 2 diabetes [2]. Another study recommends brisk walking as a preferred mode of aerobic exercise for a minimum of 30 min on most days of the week [3].

Although the positive effects of walking activity on the cardio-respiratory system and glycaemic control are established, concerns should be raised with respect to the effect on the feet, since there is a serious risk of foot complications in the presence of diabetic neuropathy (DMPN). The estimated prevalence of DMPN is nearly 50% among the diabetic population [4]. Diabetic foot complications usually follow a trend following peripheral neuropathy, beginning with ulceration [4] causing partial foot amputation (PFA) and ultimately resulting in major lower extremity amputation (LEA). Foot ulcers precede the vast majority (85%) of LEAs in patients with diabetes mellitus [5]. Soft tissue and bone infections that do not respond to vigorous local care and i.v. antibiotic therapy may require amputation [6]. In an attempt to salvage the foot for ambulation, PFA is often performed [7]. PFAs often predispose the diabetic patient to increased foot pressures and development of foot deformities, which further increase their risk of ulceration and amputation [8].

Walking activity has been quantified in some of these groups of patients with foot complications [9, 10]. Also, there is substantial literature available discussing the plantar pressure distribution in this patient population [11–13]. However, functional outcome based on measures of capacity and performance [14], along with the impact on weight-bearing, needs further investigation in the diabetic population with foot complications. Not enough is known about the advantages and disadvantages of walking, making it difficult to provide appropriate recommendations for exercise in this patient population.

Therefore we aimed to study the capacity and performance in relation to walking activity and its impact on the plantar tissues across the various groups with DMPN at sequential stages of foot complications, namely (1) DMPN with no history of further complications; (2) DMPN with unilateral current diabetic foot ulcers (DFUs) on the plantar surface; (3) DMPN with unilateral healed PFAs; and (4) DMPN with unilateral trans-tibial amputation (TTA). We predicted that the capacity and performance of walking would decrease and the potential risk of plantar injury based on peak plantar pressures would increase with the progression of foot complications.

Subjects, materials and methods

Ethical approval

The study was approved by the Cardiff and Vale NHS Trust Research & Development Office and the South East Wales Local Research Ethics Committee, UK. The investigations were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2000.

Subjects

Following written informed consent, 23 control subjects with no history of plantar ulceration, 23 subjects with unilateral current plantar ulceration (heel ulcers=5; first metatarsal [MT] head=7; second MT head=1; fifth MT head=4; hallux=4; second toe=1; fourth toe=1), 16 subjects with healed unilateral PFAs (trans-MT=5; ray=4; hallux=5; all five toes=1; first two=1), and 22 subjects with healed unilateral TTA participated in this cross-sectional study.

Patients with DFUs, PFAs and TTAs were matched on marginal distributions with respect to weight, height and BMI with the 23 control subjects. All 84 subjects were known cases of DMPN. Amputations of the ray or hallux with or without toes and trans-MT amputations were classified as PFAs for this study.

Semmes–Weinstein monofilaments were used to confirm the neuropathy status [15]. Neuropathy was considered present if the 5.07 (10 g) Semmes–Weinstein monofilament (loss of protective sensation) was not perceived in at least one of the four plantar areas tested (heel, first MT head, fifth MT head and hallux). Between five to ten trials were performed at each site [16] and the subject needed to perceive 80% of the trials to be graded as the sensation intact over that site. The site was scored 1 in the case of the presence of sensation and 0 in the case of absence of the sensation. The sum of the scores over the four sites was used to present the final sensory score over the entire foot (Table 1).

Selection criteria

Subjects within the age range of 40 to 75 years, living independently in the community, with visual acuity of a minimum of 20/40 in the better eye (pre-requisite to obtain a driving licence) and an ability to communicate without support were included. All the participants were capable of walking independently to perform their activities of daily life with or without a walking aid. However, no walking aids were used during the testing procedures. The patients with TTAs always used their artificial limb for walking. All the subjects with TTAs had completed at least 6 months following rehabilitation at the time of discharge

Table 1 Characteristics of the patients from all four groups

Subject characteristics	DMPN group (*n*=23)	DFU group (*n*=23)	PFA group (*n*=16)	TTA group (*n*=22)
Age (mean±SD)	64.48±5.75	59.74±9.55	62.13±8.83	62.86±6.08
Sex (F/M)	3/20	4/19	1/15	2/20
Type of diabetes (1/2)	12/11	3/20	7/9	6/16
Height, cm (mean±SD)	175.47±7.98	176.90±9.04	175.54±8.73	174.14±5.34
Mass, kg (mean±SD)	95.51±9.82	98.48±19.54	93.98±18.90	95.45±14.65
BMI, kg/m^2 (mean±SD)	31.11±3.37	31.47±6.19	30.5±6.12	31.42±4.21
Sensory score, min=0; max=4 (no. of subjects)				
0	4	19	11	14
1	5	3	3	1
2	12	1	1	1
3	2		1	6

Groups were matched on marginal distributions for height, weight and BMI. The plantar sensory score indicates that the patients with further foot complications such as DFUs, PFAs and TTAs were more neuropathic compared with the group with DMPN

from Artificial Limb and Appliance Centres (South Wales).

Exclusion criteria

Patients with bilateral LEAs or any major neurological and musculo-skeletal impairment other than those resulting from diabetic foot complications, for example, diabetic peripheral neuropathy or painful forms of DMPN, DFUs, PFAs or TTAs were excluded from the study. Subjects taking medication with known effects on the central nervous system, or with known dependence on alcohol and/or drugs were excluded. Patients presenting with acute symptoms of nephropathy or cardiovascular complications resulting from diabetes mellitus or any other major chronic illnesses were excluded as well.

Instrumentation and procedure

The capacity for walking was measured using the total heart beat index (THBI), which was calculated as an index of energy expenditure [17] during a 2-min walk test [18]. The patients walked at their natural self-selected speed. A heart rate monitor (Polar S8 10i; Polar Electro OY, Kempele, Finland) was used to record the total number of heart beats, and the total distance covered during the walk test was recorded. THBI was computed as the ratio of the total number of heart beats to the total distance covered [17].

Step activity monitors (SAMs) (Prosthetics Research Study, Seattle, WA, USA) were used to record the performance of daily walking activity [19]. The SAM is a reliable and valid tool for the measurement and recording of walking activity [20]. The accelerometer-based device measuring 680 × 50 × 20 mm was strapped around the subject's right leg laterally above the ankle joint and the parameters were optimised according to the height and gait characteristics of each individual subject. Subjects were instructed to wear the SAM continuously for eight consecutive days, except when bathing, showering or swimming. The number of strides every 1-min interval were recorded for a continuous 24 h over seven consecutive days. The mean average daily stride count was considered for analysis (one stride equals two [right and left] steps).

Gait velocity was chosen as a measure of gait performance and measured using a digital video camera at a sampling rate of 25 Hz. Each subject walked a distance of 12 m at their self-selected pace. Three trials were recorded for each subject [21] as they walked on level ground between two parallel calibration sticks placed 1 m apart.

The impact of walking activity on weight-bearing was studied based on the plantar pressure distribution. Maximum peak pressure (MPP) was measured during the gait measurement using the Pedar in-shoe pressure measurement system (Novel, Munich, Germany) at a sampling rate of 50 Hz. MPP reflects the absolute peak pressure during the gait cycle. All patients were measured in uniform standard footwear with appropriate shoe fillers for the patients with PFAs. Two-millimetre thick insoles available in different standard and wide sizes were calibrated using the standard calibration device with homogeneous air pressure ranging from 4 to 60 N/cm^2. Zero measurement was performed before starting the experimental measurement.

Plantar pressure data were analysed using Novel standard software version 10.33. Three trials were recorded for each subject and five mid-gait steps on the right and left foot were selected for analysis from each trial. Individual masks were created for each subject subdividing the foot into six regions, namely: heel, midfoot, medial MTs (first and second MTs), lateral MTs (third, fourth and fifth MTs), hallux, and all the toes. The plantar pressure data obtained from the affected foot of the patients with DFUs and PFAs were compared with data from the right foot of the control

Table 2 Comparison of gait velocity, daily walking activity and THBI (means±SD) of the subjects across the four groups

Walking activity	DMPN group	DFU group	PFA group	TTA group	*p* value for linear polynomial contrast
Gait velocity (m/s)	1.1+0.2	0.9+0.3	0.9+0.2	0.7+0.2	<0.001**
Daily strides (strides/day)	4,409+1,953	2,742+1,584	3,133+1,315	1,894+1,081	<0.001**
THBI (beats/min)	1.2+0.4	1.6+0.7	1.9+0.6	2.0+1.4	0.019*

*Significant; ** highly significant

group. Considering the symmetrical pattern of distal polyneuropathy affecting the feet [22] data from the right feet were considered for comparative analysis by default. We confirmed that there was no significant difference in the total MPP between the right and left foot in the control group (p=0.134).

Statistical analysis

The minimum sample size was calculated to be 23 subjects. Based on a number of gait parameters reported by Mueller et al. [23] a range was found for the standardised difference of between 1.15 and 1.57. For this power calculation a conservative estimate of the standard difference of 1 was used. A power of 0.8 and a significance level of 0.05 were used for this calculation.

No major departures from the necessary parametric assumptions were evident. Linear polynomial contrast within an ANOVA (SPSS 11) was used to investigate the trend of the gait parameters across the four groups. Considering the influence of gait velocity on MPP [24], one-way analysis of covariance was used to compare the means of the MPPs of the adjusted groups with gait velocity as a covariate [25]. Gait velocity was used as a covariate in the analysis of peak plantar pressures because slower walking speed is known to coincide with decreased pressures over some areas of the foot [26]. A significance level of 0.05 was used.

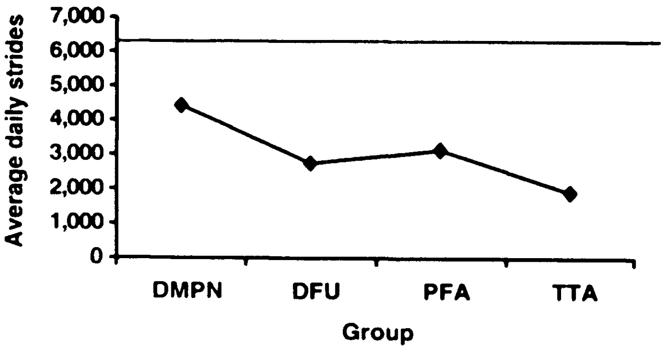

Fig. 1 The average daily stride count decreases from the control diabetic neuropathy (DMPN) group to the group with plantar ulceration (DFU), improves with the partial foot amputation (PFA) group and decreases further with the trans-tibial amputation (TTA) group. The daily walking performance of the diabetic control group is lower compared with the non-diabetic healthy subjects measured by Busse [38]. The *horizontal line* refers to the data from the reference study

Results

The subject characteristics of the four groups are presented in Table 1.

THBI, an index of energy expenditure, showed a progressively significant rise across the four groups (p=0.019), as shown in Table 2, indicating a decline in physical fitness. The average daily strides showed a significant (p=0.000) decline across the groups, demonstrating a decreasing level of activity. However, the graph related to the significant linear polynomial contrast between the groups suggests that the patients with PFAs walked more than the patients with DFUs (Table 2 and Fig. 1). Gait velocity decreased significantly across the four groups from DMPN to TTA (p=0.000).

The descriptive and inferential statistics for the MPP over the affected and the contralateral foot are presented in Table 3. A significant rise in peak pressures was noted over the total plantar area of the foot on the affected limb from DMPN to DFU to PFA group (p=0.002). Regional assessment of specific plantar areas revealed a significant rise in MPP over the midfoot region on the affected limb from DMPN to PFA group (p=0.006).

On the contralateral limb, the heel (p=0.015) and the medial metatarso-phalangeal region (p=0.040) demonstrated significant difference in peak pressures across the four groups with a significant rise in MPP over the heel (p=0.005).

Discussion

The present study aimed to investigate the functional outcome of walking activity among the four groups of patients at different stages of foot complications. THBI, average daily stride count, gait velocity and peak pressure were chosen as parameters representative of capacity and performance of walking and its impact on the diabetic foot.

The limitation of this study lies in the choice of a cross-sectional design rather than a longitudinal study. The robustness of the study would increase with a longitudinal design to investigate the variations in walking activity as foot complications progress in the diabetic population. However, considering the time-scale required for a longitudinal study and the cost involved we opted to explore our

Table 3 The descriptive and inferential statistics for the MPP (kPa, means±SD) over the affected and the contralateral foot for the four groups are presented along with the post hoc comparisons of the groups with DFUs, PFAs and TTAs with the DMPN group (controls) using gait velocity as the covariate

Foot region	DMPN group	DFU group	PFA group	TTA group	*p* (ANOVA)	*p* for linear contrast
Total						
Affected	344.5±82.9	366.9±72.6	395.7±110.1	n/a	0.006**	0.002**
Contralateral	342.8±81.3	375.6±71.1	343.0±90.0	337.9±88.7	0.091	0.179
Heel						
Affected	247.5±41.9	212.7±77.5	209.5±59.3	n/a	0.674	0.461
Contralateral	247.6±51.7	239.1±46.2	270.9±63.9	246.5±52.1	0.015*	0.005**
Midfoot						
Affected	88.2±41.9	80.8±73.4	194.9±178.7	n/a	0.005**	0.006**
Contralateral	74.4±43.2	66.3±47.1	67.2±45.0	82.6±49.4	0.680	0.623
Medial MTs						
Affected	322.1±93.6	329.6±123.5	245.9±167.5	n/a	0.167	0.565
Contralateral	322.9±88.4	367.3±88.1	307.0±103.7	306.9±99.3	0.040*	0.363
Lateral MTs						
Affected	282.5±88.5	264.0±105.6	243.0±190.7	n/a	0.904	0.964
Contralateral	298.1±78.2	277.7±72.1	248.6±54.1	240.4±84.2	0.738	0.454
Hallux						
Affected	182.2±81.4	114.2±116.2	n/a	n/a	0.100	0.100
Contralateral	177.0±52.1	157.6±83.9	146.2±109.1	165.1±113.5	0.832	0.663

*Significant; **highly significant

Medial MTs First and second metatarsal region, *lateral MTs* fourth and fifth metatarsal region, *n/a* not available

research question with a cross-sectional design. However, even a cross-sectional study design posed its own limitations when we were confronted with difficulties in recruiting adequate number of patients with PFAs. Recruitment of adequate numbers of subjects with healed unilateral PFAs was a challenge due to three major factors: (1) the lower incidence of PFAs compared with major LEAs at our centres; (2) the incidence of problems such as wound failure or progression to higher levels of amputation; and

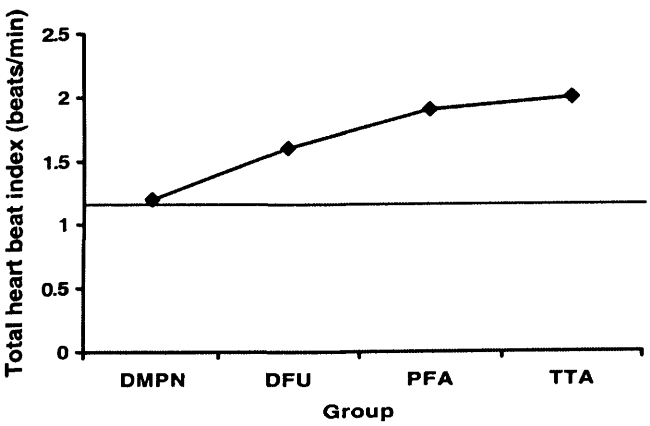

Fig. 2 The gradual rise in the mean total heart beat index (THBI) count across the four diabetic groups indicates an increase in energy expenditure. The THBI score of the control diabetic neuropathy (DMPN) group is comparable with the score of the non-diabetic healthy group presented by Hood et al. [17]. The *horizontal line* refers to the data from the reference study. DFU, diabetic foot ulcer; PFA, partial foot amputation; TTA, trans-tibial amputation

(3) the presence of acute symptoms of neurological or musculo-skeletal disorders, which might have introduced a confounding bias in the interpretation of the results. However, a reasonable sample size of the PFA group allowed us to compare the four groups statistically.

Our results showed changes in THBI, average daily stride count, gait velocity and peak pressure, demonstrating a decline in the functional capacity and performance of walking and increased risk of plantar injury with progression of foot complications.

Low cardio-respiratory fitness and physical inactivity are independent predictors of all-cause mortality in men with type 2 diabetes mellitus. Therefore it is believed that patients with type 2 diabetes should be encouraged to participate in regular physical activity [27]. Our results confirm the decline in the level of physical fitness demonstrated by increased energy expenditure across the four groups (Fig. 2). Alternatively it could be argued that walking requires more physical exertion (in terms of aerobic capacity) as the level of physical impairment progresses. Therefore the level of physical fitness and the level of physical impairment appear to be interdependent. It is hard to establish a cause–effect relationship between the two factors without a longitudinal study. Irrespectively, the steady rise in the energy expenditure indicates the greater need for improving the level of fitness as the diabetic patients progress from peripheral neuropathy to foot ulceration to minor amputations to major amputations of the lower extremity.

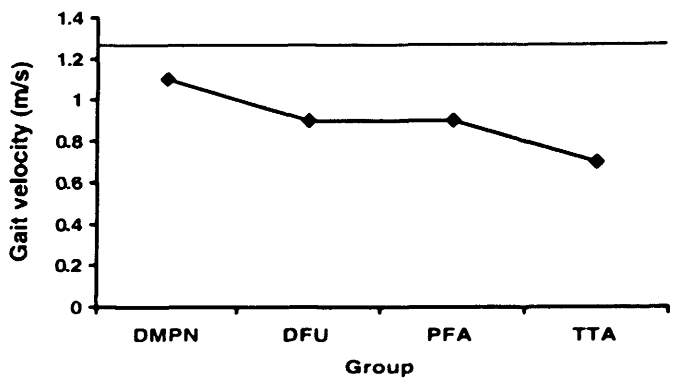

Fig. 3 The gradual decline in the mean values of gait velocity across the four diabetic groups is plotted against the *horizontal line* referring to the data from the non-diabetic, healthy group measured by Mueller et al. [23]. *DMPN* Diabetic neuropathy, *DFU* diabetic foot ulcer, *PFA* partial foot amputation, *TTA* trans-tibial amputation

In terms of the performance of walking activity, there was an overall decline in the daily walking performance with progression of foot complications from DMPN to TTA (Fig. 1). However, the graph related to the significant linear polynomial contrast between the groups suggests that the patients with PFAs walked more than the patients with DFUs. The overall decline in walking performance is in tune with the pattern noticed by Tennvall and Apelqvist [28] in the health-related quality of life (H-R QOL) among diabetic people at different stages of foot complications. Diabetic patients with minor amputations are reported to demonstrate better H-R QOL compared with patients with current ulcers, and patients with major amputations are reported to demonstrate lower H-R QOL compared with patients with minor amputations [28]. Although we could not locate any direct evidence to support the linear relationship between the volume of walking activity and H-R QOL, further research in this area would be necessary to explore the precise relationship between the two variables, if any.

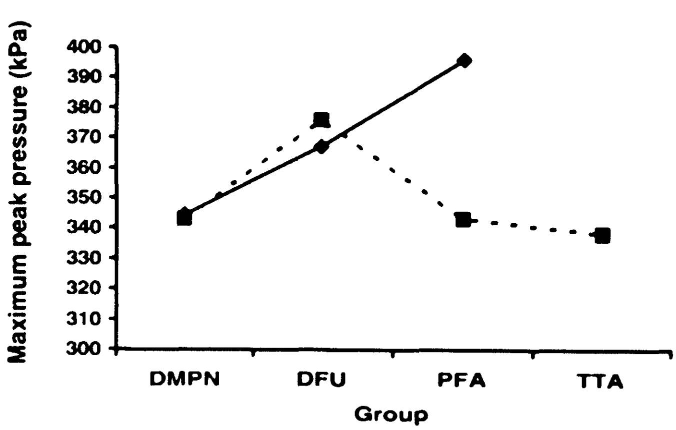

Fig. 4 The maximum peak pressure over the total surface area of the affected foot is demonstrated by the *solid line* and the contralateral foot is demonstrated by the *broken line* across the four diabetic groups. *DMPN* Diabetic neuropathy, *DFU* diabetic foot ulcer, *PFA* partial foot amputation, *TTA* trans-tibial amputation

Although our findings confirm the reduction in daily walking activity and the need for improving the physical fitness of this patient population, the plantar pressure distribution on the affected and the contralateral foot during walking needs to be considered before walking can be recommended as a safe form of physical activity to improve fitness.

People with DMPN are known to present with a slower gait pattern [29]. Our results demonstrate a progressively gradual decline in the gait velocity as we proceed through the four groups (Fig. 3) indicating a progressive deterioration in the gait pattern. Gait velocity was used as a covariate in the analysis of peak plantar pressures because slower walking speed is known to coincide with decreased pressures over some areas of the foot [26]. On the affected limb, despite the gradual fall in the gait velocity, the results demonstrate a rise in the MPP values over the total foot from DMPN to PFA (Fig. 4). Higher peak pressures are already documented in patients with DFUs and PFAs on the affected side [12, 13]. The increased plantar stress on the ulcerated foot and the reduction in the total contact area of the partially amputated foot might explain the higher average MPP values, indicating an increased risk of injury to the foot. Our findings did not demonstrate significantly increased MPP values over the fore-foot areas as reported in other studies. Although the majority of patients had fore-foot ulceration, the averaging effect of various sites of ulcers probably masked the otherwise pronounced individual peak pressures. It should therefore be noted that the findings from this study indicate the potential risk of plantar injury to the entire foot, but the study is limited in providing information necessary to indicate risk to the specific plantar area.

On the contralateral side, the surviving foot of the patients with TTAs has received attention in the past with the objective of evaluating the risk of injury [11, 30]. The authors have demonstrated in a previous study that despite walking 30% more slowly than diabetic neuropathic subjects, patients with TTAs experienced increased plantar stress on the surviving foot during walking. Adaptations in gait and level of walking activity were identified to affect the plantar pressure distribution and ultimately the risk of ulceration to the surviving foot [30].

However, little is known about the pressure distribution over the contralateral foot among the patients with current DFUs and unilateral PFAs, despite the existing risk of plantar injury due to the presence of DMPN. Our results demonstrated a significant difference in the MPP on the heel and the medial metatarso–phalangeal regions of the contralateral foot across the four groups, demonstrating a significant rise in the heel peak pressures. Although the authors resisted multiple testing because of the danger of false-positive results, it is interesting to note that the DFU group demonstrated an 8.7% rise in average total foot pressures and a 12.1% rise in average MPP over the medial MTs compared with the DMPN group, despite walking significantly more slowly. The protective mechanism adopted by the patients with DFUs to safeguard the ulcerated foot during walking, more specifically an increased push-off with the contralateral foot, might explain the compensatory increase in peak pressures on the contralateral foot.

Similarly, patients with PFAs demonstrated increased average MPP values on the heel of the contralateral foot compared with the controls. Adaptations in the gait pattern resulting from PFA can explain the increased plantar stress on the contralateral foot. Garbalosa et al. have reported a significantly greater maximum dynamic dorsiflexion range of motion during walking on the contralateral ankle compared with the ankle on the affected side following transmetatarsal amputation [31], which might result in a pronounced heel strike, explaining the greater plantar stress on the contralateral heel of the patients with PFAs in our study.

The TTA group presented with peak pressures comparable with the control group, despite a 39% slower walking speed. Given the decreased capacity and performance of walking in this patient group, one might be tempted to increase the volume of walking activity. But the pressure picture suggests cautious implementation of rehabilitation programmes. Efforts to restore a near normal volume of ambulation in this patient population might increase the risk of plantar injury due to the rise in moderate repetitive stress, which is as equally instrumental as abnormally higher instantaneous stress in the development of plantar ulceration [32].

In summary, all the four groups in this study are already at risk of plantar injury due to the presence of DMPN [33]. Further complications, such as plantar ulceration, PFAs and TTAs, increase the risk of plantar injury in this patient population during walking. However, since walking is an integral component of activities of daily life [34], we suggest maintenance of essential daily walking in protective footwear with foot care [35, 36] and appropriate modifications in the gait pattern to reduce the MPP [37].

Concurrently the vital need to optimise physical fitness in this population could be addressed with partial weight-bearing or non-weight-bearing aerobic exercises as supplementary safe options. However, further research is needed to arrive at a specifically tailored aerobic exercise programme with equal emphasis on foot care and physical fitness for this patient population, which presents with specific needs at different stages of foot complications.

Conclusion

The diabetic foot is already at risk of plantar injury in the presence of neuropathy. With consequent stages of foot complications, the risk of injury increases further. Although the positive effects of walking on the cardio-respiratory system and glycaemic control are established, its impact on the neuropathic foot, leading to further complications, does not support its prescription as the solitary best option to improve physical fitness in the diabetic population. In order to optimise the functional outcome of walking without paying the price of increased risk of plantar injury to the diabetic foot, maintenance of essential walking in protective footwear along with appropriate modifications in the gait pattern and adequate foot care is recommended. Diabetic patients with plantar ulceration and PFAs need protection not only on the affected foot, but also on the contralateral foot to prevent the increased risk of plantar injury. Ambulation programmes among diabetic patients with TTA should, of necessity, be implemented with caution.

Concurrently, alternative forms of partial or non-weight-bearing aerobic exercises could be considered supplementary to essential walking exercise to improve the level of physical fitness and glycaemic control of this patient population.

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R. W. M. van Deursen, the corresponding author for this paper, has full access to the data in the study and had the final responsibility for the decision to submit the paper for publication.

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Letter to the Editor

Difficulties in recruiting subjects with partial foot amputations for kinesiological research

To the Editor,

We are reporting the difficulties encountered in the recruitment of patients with partial foot amputations (PFA) following diabetic neuropathy (DMPN) for kinesiological research during an attempt to study the functional outcome following healed unilateral PFA in subjects with DMPN. Amputations of the hallux, ray and trans-metatarsal amputations were collectively classified as PFA for our study.

This kinesiological study included kinetic (study of forces) and kinematic (study of motion irrespective of the forces which govern the motion) analyses of functional activities such as sit-to-stand, standing and walking. Therefore, it was necessary to exclude patients with bilateral lower extremity amputations (LEA), gross neurological and musculoskeletal impairments apart from those related to DMPN and painful forms of DMPN to minimise any confounding bias in the interpretation of the results.

Based on power calculations a minimum number of 23 subjects was required for this study ($\alpha = 0.05$, $1 - \beta = 0.80$).

Patients from two major NHS Trust hospitals and three podiatry and two diabetic foot clinics were screened for recruitment. At the first hospital, 32 subjects underwent PFA over a 2-year period. PFA were performed as primary procedures on 25 (25/32) subjects, of those 9 had diabetes (DM). One (1/9) subject attained healing, 6 (6/9) subjects with DM did not heal and 2 subjects underwent ipsi-lateral TTA (76 and 80 weeks, respectively) later. Seven (7/32) subjects underwent PFA as a secondary procedure (the primary procedure in these patients was vascular reconstruction) and out of those four subjects had DM, of those four, three subjects did not heal and one refused to participate in the study.

At the second hospital, 18 patients with diabetes related PFA were identified of which 2 subjects remained unhealed, 4 subjects developed contra-lateral LEA following PFA, 6 subjects developed ipsi-lateral DFU following PFA, 1 subject was severely affected by Osteoarthritis, 1 subject suffered from partial blindness and 4 subjects did not respond to the invitation. Effectively, between the two hospitals from the 50 patients identified over a 19-months period, one ended up participating in our study. Another 15 subjects with healed PFA were identified through the various clinics.

This challenging recruitment process highlights the difficulty in finding diabetic subjects with healed unilateral PFA. This could be attributed to many factors: (i) very low incidence of PFA compared to major LEA among diabetic subjects in South Wales (unpublished data) which was concurrent with the low incidence of foot amputations reported previously in the UK and USA [1,2]. (ii) Prolonged period of wound healing demonstrated by diabetic subjects following PFA: one subject from our centre had a healing time of 24 weeks. Although, we did not have this information for the other 15 participants, the time duration was similar to the previously reported average healing time, i.e. 29 weeks [3]. (iii) Increased risk for ulceration and re-amputation in diabetic patients with PFA as reported earlier [4]. Of the 27 diabetic subjects from both the centres 22.2% underwent re-amputation (2/27 ipsi-lateral amputations, 4/27 contra-lateral amputations) and 22.2% of subjects developed ipsi-lateral DFU.

Kinesiological studies involving people with PFA require complete healing following an amputation. The presence of a wound could confound the results since it can produce movement alterations in addition to the changes already produced by PFA. On the other hand, the challenge to recruit adequate numbers affects the statistical analysis of the results. Therefore two-to-one (Controls: PFA) matching of subjects and prudent use of statistical tools to accommodate for unequal group sizes appear to be appropriate strategies in such cases.

However, the low percentage of diabetic people with healed PFA and the rapid succession of further complications raise serious concerns. These facts underline the need for further research into improving the healing process and preventing further complications.

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R.V. Kanade
R.W.M. van Deursen *
Research Centre for Clinical Kinaesiology, Department of Physiotherapy, School of Healthcare Studies, Cardiff University, Ty Dewi Sant, Heath Park, Cardiff CF14 4XN, UK

Keith Harding
Patricia Price
Wound Healing Research Unit, School of Medicine, Cardiff University, Cardiff, UK

* Corresponding author. Tel.: +44 2920 744587; fax: +44 2920 748329.
E-mail address: **vandeursenr@cardiff.ac.uk** (R.W.M. van Deursen)

Daily walking activity following partial foot amputations in diabetic people

[1]Rajani V Kanade; [1]Dr. Robert van Deursen; [2]Prof. Patricia Price; [2]Prof. Keith Harding
Research Centre for Clinical Kinaesiology, Physiotherapy & Wound Healing Research Unit

Background: The influence of partial foot amputations (PFA) on lower limb function has not been researched sufficiently. Therefore, the aim of this study was to explore the impact of PFA on the capacity and performance of walking and its implications on the affected and sound lower limbs.

Methods: Fourteen subjects with healed unilateral PFA with DN (Trans-metatarsal amputation, n=4; Ray amputation, n=5; Hallux amputation, n=5) were compared to 28 matched control subjects with DN and no history of plantar ulceration. All subjects signed an informed written consent and were matched for mass, height, age and type of DM (I/II) . Gait parameters were measured using a digital video camera. Plantar maximum peak pressure (MPP) during walking was recorded using the Pedar in-shoe system. Capacity of walking was measured using a Polar Heart Rate Monitor to calculate Total Heart Beat Index (THBI) and the performance of walking was recorded using the Step Activity Monitor.

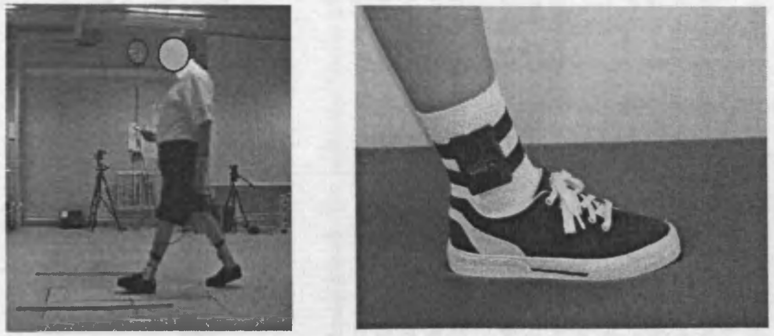


Figure 1: Plantar pressure measured with pressure insoles in the shoes (left). Number of steps measured with an activity monitor worn on the right ankle (right).

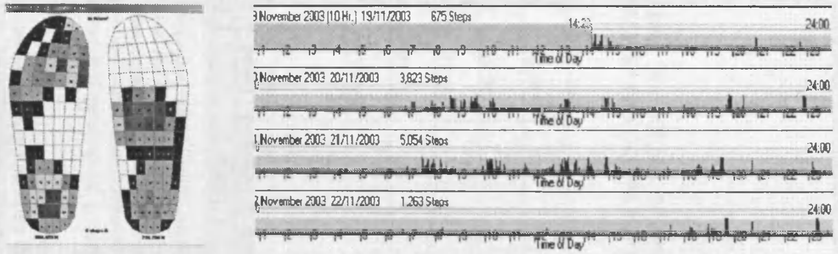


Figure 2: Pressure distribution over foot with trans-metatarsal amputation (left). Activity pattern measured over 3 days on the same patient (right).

Results: The PFA group walked with significantly slower gait velocity ($P<0.01$) and shorter strides ($P<0.001$), but higher peak plantar pressures occurred: in particular, the mid foot region of the amputated foot showed significantly higher MPP values ($P<0.05$) and the contra-lateral forefoot (MPP; $P<0.01$). Average daily walking was less for the PFA group but not significantly ($P=0.094$). Energy expenditure (THBI) was significantly greater in the PFA group ($P<0.01$) compared to the control group.

Discussion: Higher plantar pressures despite walking significantly slower suggests a potential risk of plantar injury. Increased energy expenditure indicates reduced cardiovascular fitness which could affect activity levels and functional performance.

Required interventions:

- Protection of the amputated foot
- Protection of the contra-lateral forefoot
- Alternate forms of aerobic exercises to decrease energy expenditure & improve walking performance.

What happens to the contra-lateral foot following diabetic foot amputations?

Rajani.V.Kanade (1), Robert.WM.Van Deursen (1), Patricia.E.Price (2) Keith.G.Harding (2)

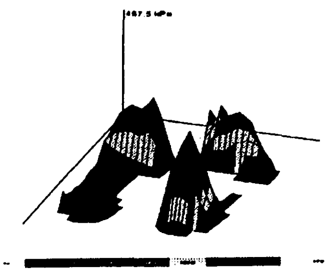
1. Research Centre for Clinical Kinaesiology, Cardiff University, Wales, UK
2. Wound Healing Research Unit, Cardiff University, Wales, UK

Background: The pathomechanics of diabetic foot amputations are already documented in the literature. However the contra-lateral changes has received less attention. Therefore this study was aimed to investigate changes occurring in the contra-lateral limb following a partial foot amputation (PFA).

Methods: 16 patients with PFA (Transmeta-tarsal=5; Ray=5; Hallux=4; Hallux+toes=2) and diabetic neuropathy (DMPN) were matched with 23 patients with DMPN for height, mass and age. Net joint moments at hip and ankle were calculated using a Kistler Force platform and a 512 Vicon Kinematic system. Plantar pressure distribution during walking (with shoe filler) was recorded using the Pedar in-shoe system. Gait characteristics and plantar pressures (co-variate=gait velocity) were compared between the 2 groups using ANOVA and were compared within each group using a paired sample t test.

Findings: Patients with PFA walked with reduced gait velocity ($p \leq 0.001$) and decreased ankle moments ($p \leq 0.001$) on the amputated limb compared to the DMPN group. The PFA group showed higher pressures over the mid-foot ($p<0.05$) of the amputated limb and the heel ($p<0.034$) of the contra-lateral limb compared to the controls.
Within the PFA group the ankle plantar flexor moments ($p \leq 0.001$) were higher on the contra-lateral-limb than the amputated limb. Also the MPP ($p<0.05$) and the PTI ($p<0.05$) were significantly higher over the mid-foot of the amputated limb compared to the contra-lateral limb. However the MPP over the heel ($p<0.05$) of the contra-lateral limb was higher compared to the amputated limb. The DMPN group did not show this variation between the two sides during walking.

Figure 1: 3D plantar pressure picture of a typical patient with left trans-metatarsal amputation demonstrating higher MPP over the right heel.



Interpretation: Deformed and shortened feet with inadequate plantar flexor lever arm on the amputated limb can explain the decreased ankle moment observed (Mueller et al 1998). The higher plantar pressures over the mid-foot could be explained by the reduced surface area. Although not measured, the partially amputated foot may have less dynamic ankle dorsiflexion ROM during gait as seen in patients with trans-metatarsal amputations (Garbalosa et al. 1996). Presence of neuropathy in both groups confirms the fact that the gait deviations are likely to be an effect of amputation rather than neuropathy as speculated by Mueller et al (1998).
There were no evident gait compensations at the hip and the knee joints but patients with PFA demonstrated gait asymmetry at the ankle. On the contra-lateral limb they walked with greater ankle moments in an apparent attempt to compensate for the decreased push-off on the affected limb. Also the peak pressures were higher over the heel. This may indicate a potential risk of plantar tissue injury on the contra-lateral foot. Therefore during treatement and rehabilitation following diabetic PFA care must be taken to protect the intact foot.

Table 1: Mean values and S.D. for the ankle peak plantar flexor moment; hip peák extensor moment; peak pressure over the total foot, heel and midfoot for the affected and contra-lateral limb of the PFA group. Data for the same parameters from the right limb of the patients with DMPN are presented for reference.

	PFA			**DMPN**
	Affected limb Mean (SD)	Contra-lateral limb Mean (SD)	Paired t-test	Mean (SD)
Ankle moment (N.m)	83.0 (21.7)	118.5 (26.4)	p<0.01	128.0 (25.2)
Hip moment (N.m)	54.0 (17.9)	59.7 (18.9)	0.244	66.9 (19.5)
MPP: total (kPa)	400.3 (108.0)	345.8 (87.6)	0.064	356.4 (88.9)
MPP: heel (kPa)	217.2 (65.0)	278.2 (68.3)	p<0.05	251.8 (39.5)
MPP: midfoot (kPa)	184.2 (177.7)	65.9 (43.8)	p<0.05	82.9 (41.1)

References:

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O25

Daily walking activity following partial foot amputations in diabetic people

[1]Kanade RV, [2]Price PE, [2]Harding KG, [1]van Deursen RWM
[1]Research Centre for Clinical Kinaesiology, [2]Wound Healing Research Unit, Cardiff University, Wales, UK

Background: Altered plantar pressure distribution is a common area of concern following partial foot amputations (PFA). However, there is limited information related to the influence on the performance of the affected and sound lower limb (LL). Therefore, the aim of this study was to explore the impact of PFA on the capacity and performance of walking and its implications on the affected and sound LL.

Methods: In this ongoing study, 14 subjects with healed PFA with DN (Trans-metatarsal amputation, n=4; Ray amputation, n=5; Hallux amputation, n=5) were compared to 28 matched control subjects with DN and no history of plantar ulceration. All the subjects signed an informed written consent. Gait parameters were measured using a digital video camera, Kistler Force platform and 512 Vicon Kinematic system. Plantar pressure distribution during walking was recorded using the Pedar in-shoe system. Capacity of walking was measured using the Total Heart Beat Index (THBI) with the Continuous Polar Heart Rate Monitor and the performance of walking was recorded using the Step Activity Monitor. Patient's participation in physical and social life was assessed with self-administered SF-36.

Results: The PFA group walked with significantly slower gait velocity (p=0.006), shorter strides(p=0.000) and higher peak pressures (MPP; p=0.005) over the affected foot. The mid foot region of the amputated foot showed significantly higher regional MPP (p=0.025) and pressure-time integral (PTI; p=0.032) values. Differences in average daily strides between the two groups were non-significant (p=0.094) but there was greater energy expenditure in the PFA group (p= 0.001) compared to the control group. The PFA group showed higher peak joint moments at ankle (p= 0.004) and hip
(p= 0.031) on the sound side compared to the affected side.

Discussion: Higher MPP over the entire amputated foot along with higher MPP and PTI values over the mid foot region of the amputated foot despite walking significantly slower suggest a potential risk of plantar injury. Considering the asymmetrical gait pattern, rehabilitation measures need to safeguard the sound LL in addition to protection of the amputated foot during walking. Also, our findings indicate the need for appropriate aerobic training aimed to improve the capacity and performance of walking activity to maximise functional outcome following PFA.

O24

Functional outcome in people with trans-tibial amputations related to diabetes

[1]Kanade RV, [2]Price PE, [2]Harding KG, [1]van Deursen RWM
[1]Research Centre for Clinical Kinaesiology, [2]Wound Healing Research Unit, University of Wales College of Medicine, Cardiff, UK

Background: Diabetic neuropathy frequently leads to ulceration and these patients have an increased risk of lower limb amputation. Limited knowledge exists on the functional outcome at these various stages of the process. The aim of this study is to investigate the different aspects of functional outcome/mobility of diabetic people with trans-tibial amputations (TTA).

Methods: In this ongoing study, twelve subjects with diabetic neuropathy and unilateral trans-tibial amputations were compared with 16 matched control subjects with diabetic neuropathy and no history of plantar ulceration. Informed consent was obtained and functional status was assessed based on the fundamental activities of mobility, largely focussed on walking. Patient's perception of mobility was assessed with a self administered Rivermead Mobility Index (RMI). Plantar pressure was measured with the Pedar in-shoe system while participants walked at their natural pace. Gait parameters were measured by digital video. Physical activity was recorded using Stepwatch Activity Monitors and Total Heart Beat Index (THBI, as an indicator of energy expenditure) was measured with a Continuous Polar Heart Rate Monitor.

Results: Gait velocity, stride length, average daily strides and RMI were significantly reduced in the TTA group. Though, the THBI and plantar cumulative stress was higher in the TTA group, the differences between the two groups were not significant. Also in the TTA group, function of the surviving foot showed a significantly higher pressure-time integral over the heel and first-second metatarsal regions and a significantly decreased average velocity of centre of pressure; however, no significant differences were found in peak pressure over the same regions.

Table 1: Summary of primary results

	Control group Mean (SD)	**TTA group** Mean (SD)	p
Gait velocity (m/s)	1.06 (0.21)	0.79 (0.16)	0.001*
Stride length (m)	1.26 (0.13)	1.03 (0.13)	0.000*
RMI (score) - median	15 (9-15)	11.5 (8-14)	0.001*
Average Daily strides	3882 (1906)	2317 (1113)	0.014*
Total pressure time integral (kPa.s)	136.1 (24.0)	181.05 (39.4)	0.001*
Plantar cumulative stress (MPa /day)	521.7 (243.9)	434.2 (214.2)	0.343
Avg vel of Centre of Pressure (m/s)	0.31 (0.06)	0.26 (0.03)	0.005*
Pressure time integral 1-2 MT (kPa.s)	76.1 (22.2)	107.8 (48.0)	0.029*
Peak pressure 1-2 MT (kPa)	284.2 (74.6)	311.7 (114.0)	0.491
THBI (beats/m)	1.33 (0.55)	1.54 (0.46)	0.290

* Significant ($p \leq 0.05$)

Discussion: The group with trans-tibial amputation walked slower with shorter strides coinciding with reduced daily physical activity assessed from objective quantification and subject's own perception of level of mobility. The question, whether reduced functional capacity and mobility in people with trans-tibial amputations is substantially limiting their participation in everyday living, still needs to be addressed. Despite reduced physical activity, the surviving foot may be at increased risk of plantar ulceration. To improve the functional outcome during rehabilitation it is essential that all these relevant dimensions are considered.

RISK OF PLANTAR ULCERATION TO THE SURVIVING FOOT IN THE PATIENTS WITH DIABETIC NEUROPATHY FOLLOWING TRANS-TIBIAL AMPUTATION

Rajani V. Kanade (1), Patricia E. Price (2), Keith G. Harding (2), Robert W. van Deursen (1)

1. Research Centre for Clinical Kinaesiology, University of Wales College of Medicine, UK
2. Wound Healing Research Unit, University of Wales College of Medicine, Cardiff, UK

BACKGROUND

Following unilateral amputation in diabetes, there is a 50% incidence of amputation to the contra lateral limb within four years (Ebskov, 1980). The aim of this study is to investigate plantar loading of the surviving foot.

METHODS

Twelve subjects with diabetic neuropathy and unilateral trans-tibial amputations (TTA) were compared with 16 matched control subjects with diabetic neuropathy and no history of plantar ulceration. Plantar pressure was measured with the Pedar in-shoe system while the participants walked at their natural pace. Gait parameters were measured by a digital camcorder. (van Deursen, 2001). Physical activity was recorded using the Stepwatch Activity Monitor (Shepherd, 1999).

FINDINGS

Table 1 shows that total pressure time integral was significantly higher in the TTA group compared to controls. Average daily step count and gait velocity were significantly lower. Plantar cumulative stress was not significantly different between groups. Heel and first-second metatarsal regions showed significantly higher pressure-time integral values ($p=0.000$ and $p=0.029$ respectively) but no significant differences in peak pressure were found ($p=0.525$ and $p=0.491$ respectively).

INTERPRETATION

Despite walking substantially slower, the trans-tibial amputation group did not differ in plantar peak pressure values compared to the control group but showed increased pressure time integral values over regions normally at risk of ulceration. However, plantar cumulative stress was not different between groups because of reduced activity levels in the trans-tibial amputation group. Adaptations in gait and activity levels affect plantar pressure and the risk of ulceration in the surviving foot. Rehabilitation to increase mobility should consider implications for plantar loading and risk of ulceration to the surviving foot.

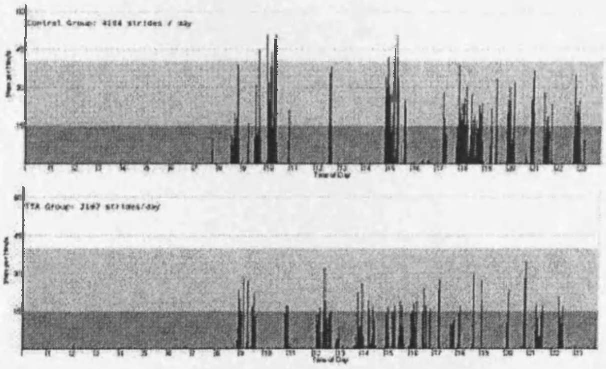

Figure 1: Typical 24 hour physical activity pattern (strides recorded every minute) of a subject from the control group (top graph: 4184 strides/24 hours) and the TTA group (bottom graph: 2107 strides/24 hours).

	Control group Mean (SD)	TTA group Mean (SD)	p
Total PTI	136.1 (24.0)	181.1 (39.4)	0.001*
Daily strides	3882 (1906)	2317 (1113)	0.014*
G Vel	1.06 (0.21)	0.79 (0.16)	0.001*
PCS	521.7 (243.9)	434.2 (214.2)	0.343
PP 1-2 MT	284.2 (74.6)	311.7 (114.0)	0.491
PTI 1-2 MT	76.1 (22.2)	107.8 (48.0)	0.029*

* Significant ($p<0.05$)

Table 1: Summary of primary results (means, standard deviations and p-values).

PTI → Pressure Time Integral (kPa.s)
Daily strides → Average Daily strides (strides/day)
G Vel → Gait velocity (m/s)
PCS → Plantar Cumulative stress (MPa/day)
PP → Peak Pressure (kPa)
1-2 MT → First & Second Metatarsal Region

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