THE UNIVERSITY of ADELAIDE

Hand Conditions Associated with Diabetes:

an observational study characterising hand function

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Discipline of Medicine

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"I love a hand that meets my own with a grasp that causes some sensation."

Samuel Osgood (1747 – 1813, American Politician)

ABSTRACT

In Chapter 1 of this thesis, I review the literature relating to the hand syndromes associated with diabetes. I describe their unique clinical features and current treatment options. I consider how these hand syndromes may contribute to physical disability in diabetes and formulate questions relating to the degree and the course of this disability.

In Chapter 2, I describe and discuss the rationale for selecting the methods used to measure hand function. The methods used to measure disability and quality of life from the individual's perspective and evaluate motor and sensory impairments of the hand are explained. Other data that was collected, such as body weight, height and information on diabetes duration and control, are discussed. The sample size required to detect a change in hand function is calculated and the clinics from which study participants were recruited are outlined.

In Chapter 3, I describe the characteristics of the sample of adults with diabetes and the associated hand syndromes at their first assessment. My analysis of the factors that predicted hand disability at the initial presentation in this heterogeneous group is presented.

In Chapters 4, I describe the change in hand function measured over the second and third assessments and determine the factors that were associated with this change. My analysis is extended to examine differences between the dominant and non-dominant hands and between men and women.

In Chapter 5, I consider the precision of measures of hand function and discuss how this affected the data obtained. Minimal detectable changes are analysed and recommendations regarding hand assessments are made.

In Chapter 6, I summarize the evidence that carpal tunnel syndrome and trigger finger contributed to hand disability in adults with diabetes. In addition to specific treatment strategies for these disorders strategies to address broader health issues are recommended. A greater emphasis should be given to strengthening the upper limb and implementing strategies to address physical inactivity and obesity in adults with diabetes.

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DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Christine Redmond and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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* **Hand syndromes associated with diabetes: impairments and obesity predict disability.**

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Christine Redmond

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Work published during the period of this research.

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LIST OF ABBREVIATIONS

AGE	Advanced Glycosylation Endpoint
BMI	Body Mass Index
CI	Confidence Interval
CID	Clinically Important Difference
CTS	Carpal Tunnel Syndrome
DASH	Disabilities of the Arm, Shoulder and Hand
DD	Dupuytren's Disease
DM	Diabetes Mellitus
ES	Effect Size
HbA1c	Glycosylated haemoglobin
GH	General Health: general health perceptions
ICC	Intraclass Correlation Coefficient
IQR	Inter-Quartile Range
LJM	Limited Joint Mobility
MCS	SF-36: Mental Component Summary
MDC	Minimal Detectable Change
MH	Mental Health - psychological distress and wellbeing
PCS	SF-36: Physical Component Summary
PF	Physical Function: limitations in physical health because of health problems
RE	Role Emotional: limitations in usual role activities because of emotional problems
RP	Role Physical: limitations in usual role activities because of physical health problems
SD	Standard Deviation
SF	Social Functioning: limitations in social activities from physical or emotional
SF-36v2	Short Form 36-item health survey (version 2)
SRM	Standardized Response Mean
TF	Trigger Finger
VT	Vitality: energy and fatigue
WEST	Weinstein Enhanced Sensory Test

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CHAPTER 1. LITERATURE REVIEW

1.1 Introduction

Hand syndromes are common in diabetes (Ardic et al. 2003; Arkkila & Gautier 2003; Cagliero et al. 2002; Fraser et al. 1979; Renard et al. 1994; Sturfelt, Leden & Nived 1981). Limited joint mobility is considered specific to diabetes and carpal tunnel syndrome, trigger finger and an atypical presentation of Dupuytren's Disease have a greater prevalence in diabetes. The mechanisms behind their development are uncertain but it is currently thought that the disease process of diabetes can affect the amount and quality of the connective tissues and make the hand's peripheral nerve supply susceptible to damage. Differences in the clinical presentation, progression or treatment outcomes that distinguish their presentation in diabetes are reviewed.

The literature contains apparent contradictions. Hand stiffness in children with type 1 diabetes, called the syndrome of limited joint mobility, has been described as "painless, nonresponsive to physical therapy, and nondisabling [sic]" (Rosenbloom 1989). We found this assertion surprising as there was no evidence provided to support this view. In contrast, there were descriptions of adults with limited joint mobility, where "stiffness, weakness, clumsiness and decreased job performance may become major problems" (Kapoor & Sibbitt 1989). It seemed that while children may adapt their functioning to a loss of mobility, somewhere along life's stages these contractures could become progressively symptomatic in some individuals. As these consequences are poorly recognised, there is little research aimed at finding effective treatments.

Improving our understanding of these disorders is timely. The prevalence of diabetes is rising, with multiple factors influencing this, including improved life expectancy, earlier age of onset and an aging population, but a major factor is the increase in incidence of type 2 diabetes as a consequence of increasing rates of obesity (Colagiuri et al. 2005; Dunstan et al. 2001). If the predicted trends are realised, then increasing numbers of adults with diabetes will develop potentially debilitating hand disorders.

It is recognised that diabetes can be associated with physical disability and weakness, which could broadly influence the clinical presentation of these hand

conditions. The overall health of an individual should be considered when determining factors that may be implicated in reduced hand function and contribute to limitations in daily activities.

In order to understand the consequences of these hand disorders and evaluate the effectiveness of interventions, these conditions should be studied with a range of outcome measures. Objective measures of impairment and patient-oriented measures should be included to measure the severity of symptoms, functional status and overall health (Liang et al. 1991; Wright 1999). By measuring underlying impairments and the functional status separately, the relationship between the two can be determined, rather than inferred (Penta, Thonnard & Tesio 1998) and the possibility for adaptation explored. Important baseline variables, such as demographic data, that may be associated with functional status should also be measured (Levine et al. 1993). Additional clinical examination that is applicable to the hands includes evaluating the performance of tasks and assessing dexterity (Schuind et al. 2003).

Collecting data to interpret the presentation, plan management and set realistic treatment goals are everyday clinical practices. However, could new patterns and determinants of hand function be identified in adults with diabetes by assessing the hands using a broad selection of standardised measures?

The purpose of this study was to develop and apply a hand assessment in adults with diabetes-related hand disorders, in order to investigate problems when undertaking everyday activities, and to determine if neuromuscular impairment or other factors were related to these difficulties. This assessment would use standardised methods to help report results and be designed to identify and highlight deficits in ways that are meaningful to both clinicians and patients (Amadio 2001). It would allow monitoring of progress, could allow comparisons with other studies of these hand disorders or other musculoskeletal conditions and could potentially offer guidance in rehabilitation or surgical indications.

1.2 Physical limitations and disability in diabetes

Diabetes is a chronic disease that affects many systems in the body and can reduce a person's physical health and quality of life. An increasingly important consequence of diabetes is the development of physical limitations (Bruce, Davis &

Davis 2005; Gregg et al. 2000; Gregg et al. 2002; Maggi et al. 2004) and it is useful to consider the hand conditions associated with diabetes within the context of these wider influences.

A broad range of impairments, diabetes complications and comorbidities have been implicated as contributing to physical decline and disability and their impacts may be cumulative. They include muscle weakness and physical inactivity, the presence and severity of neuropathy, peripheral vascular disease, coronary heart disease, visual impairment, depression and obesity (Gregg et al. 2002; Resnick et al. 2002; Sayer et al. 2006; Volpato et al. 2002). Older adults and those with longstanding diabetes are more likely to have disability, partly attributed to developing late complications of diabetes (Songer 1995).

Women may be affected more frequently and more severely by physical limitations (Ryerson et al. 2003) and obesity may have a greater negative impact in women. Obesity was associated with greater difficulties in mobility and strength in women compared to men, resulting in more difficulties with activities, including those requiring pushing and lifting (Wray & Blaum 2001).

Most studies have focussed on limitations of mobility but there is some support for limitations affecting the hands having similarities to limitations in mobility. Muscle weakness, neuropathy, obesity or long duration of disease has been associated with limited hand function in diabetes (Cederlund et al. 2009; Redmond et al. 2009; Savas et al. 2007). Difficulties with mobility have predicted the development of difficulties with activities of daily living (Bruce, Davis & Davis 2005), which suggests similar underlying causes or that limitations in daily activities can result from limited mobility.

1.3 Muscle weakness in diabetes

It is becoming increasingly recognised that diabetes is associated with muscle weakness. This affects the upper limbs (Cetinus et al. 2005; Ozdirenc, Biberoglu & Ozcan 2003; Park et al. 2006; Savas et al. 2007; Sayer et al. 2005) and the lower limbs (Andersen 1998; Andersen et al. 2004; Ozdirenc, Biberoglu & Ozcan 2003; Park et al. 2006).

A number of different factors may contribute to the development of muscular weakness. In type 1 diabetes, periods of acute hyperglycaemia reduce muscular strength (Andersen, Schmitz & Nielsen 2005). In type 2 diabetes, structural and metabolic changes including increased fat infiltration and changed proportions of muscle fibre types occur in insulin resistant muscles. Consequently, glucose is transported and utilised less efficiently during exercise (Nyholm et al. 1997; Vaag et al. 1992; Willey & Singh 2003), which could reduce muscular strength. Physical inactivity and hyperglycaemia could both contribute to muscle weakness in type 2 diabetes. While grip strength has been shown to be related to HbA1c (Cederlund et al. 2009) and impaired glucose tolerance (Sayer et al. 2005) in some studies, it has also been unrelated to HbA1c in others (Andersen et al. 2004; Savas et al. 2007). The diabetic complication of peripheral neuropathy can also contribute to weakness due to the loss of muscle mass (Andersen et al. 2004; Strotmeyer et al. 2009).

1.4 Limited joint mobility

The syndrome of limited joint mobility is characterised by thickening of the periarticular tissues and skin and shortening of the forearm flexor muscles and tendons (table 1.1). This leads to finger stiffness of the interphalangeal joints of the fingers, initially affecting the little finger and, over time, extending radially to the other fingers, or to more proximal joints (Grigic et al. 1976; Kapoor & Sibbitt 1989; Pincelli et al. 1997; Rosenbloom et al. 1981). It has also been called diabetic cheiroarthropathy, diabetic hand syndrome or diabetic stiff hand. It became recognised as a painless limitation in children with type 1 diabetes and was considered of particular interest because it could indicate an increased risk of developing microvascular complications (Grigic et al. 1976; Rosenbloom 1989; Rosenbloom et al. 1981). Limited joint mobility has been associated with retinopathy and nephropathy in type 1 diabetes and cardiovascular disease in type 2 diabetes (Arkkila, Kantola & Viikari 1994, 1997; Frost & Beischer 2001).

Table 1.1 Clinical examination signs for diagnosing the syndrome of limited joint mobility

THE SYNDROME OF LIMITED JOINT MOBILITY IN DIABETES
Positive "prayer sign"
Shortening of forearm flexor muscles and tendons
Thickened, waxy skin
Reduced ability to pinch skin on dorsum of hand
Finger oedema
Bilaterally impaired finger extension, which can be graded (Rosenbloom et al. 1981):
Nil or equivocal: Impaired extension of little finger IP joints can be a normal variant
Mild: Impaired extension of one or two IP joints; or only MCP joints; or only wrists
Moderate: Impaired extension of three or more IP joints; or impaired extension of an IP joint with impaired extension of MCP joints or wrists
Severe: Hand deformity at rest; stiffness of elbows, shoulders , cervical spine or ankles
Impaired finger flexion

Limited joint mobility is diagnosed by examination of active and passive finger joint range of finger extension and by the "prayer sign", where the fingers and palms cannot be opposed with the wrists extended (fig 1.1). Thickening of the skin may make it difficult to pick up a pinch of skin on the dorsum of the hand (Grigic et al. 1976). In longstanding limited joint mobility, impaired finger flexion can restrict function (fig 1.2).

Figure 1.1 Positive prayer sign

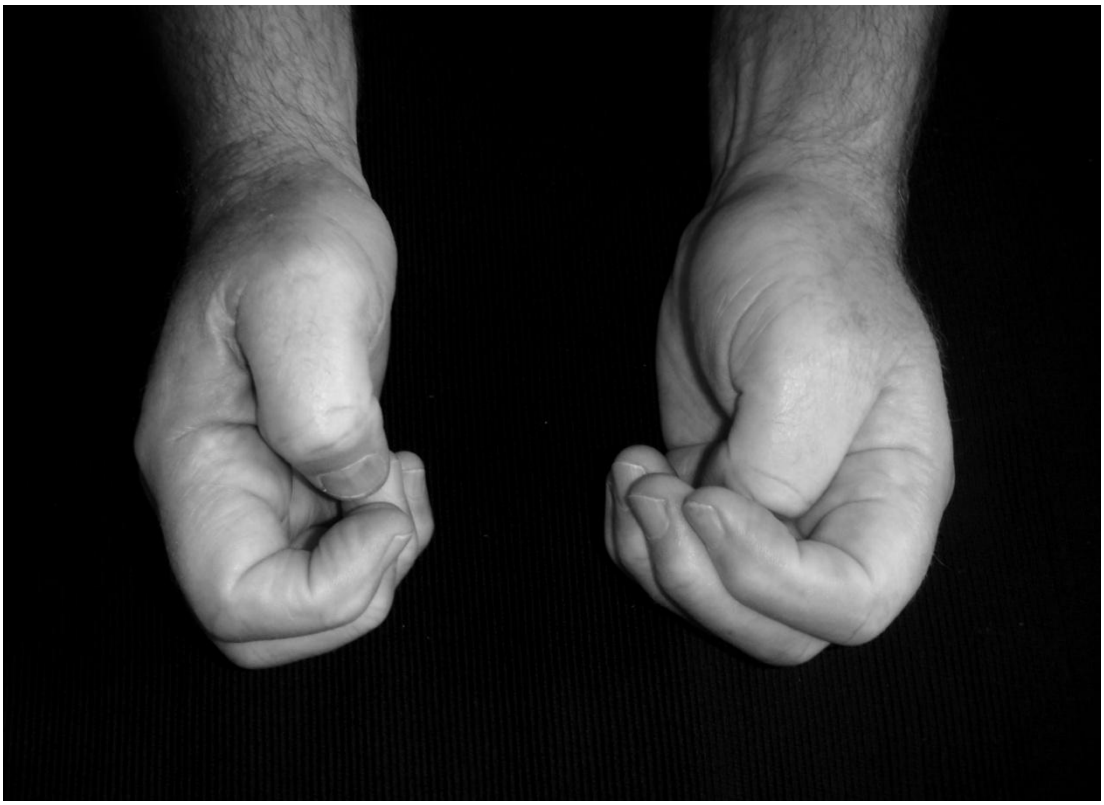

Figure 1.2 Restricted finger flexion can be associated with severe limited joint mobility.

1.4.1 PREVALENCE

Limited joint mobility appears to be a frequent clinical condition in diabetes. The reported prevalence has ranged from 7% to 58% (Ardic et al. 2003; Arkkila, Kantola & Viikari 1994; Cagliero et al. 2002; Frost & Beischer 2001; Infante et al. 2001; Lindsay et al. 2005; Pal et al. 1986; Rosenbloom et al. 1981), with some of this wide variation due to differences in definition, the precision of measurement and whether early stages of stiffness are detected (Clarke, CF, Piesowicz & Spathis 1990; Pal et al. 1986).

1.4.2 ASSOCIATED FEATURES

In adults, limited joint mobility is associated with the duration of diabetes (Campbell et al. 1985; Slama et al. 1985) and older age (Slama et al. 1985) but has not been directly related to the control of diabetes. However, there is some indirect evidence that limited joint mobility is related to long term effects of hyperglycaemia as improved standards of diabetes care and control of hyperglycaemia has reduced the prevalence of limited joint mobility in children with type 1 diabetes (Infante et al. 2001; Lindsay et al. 2005).

In adults, limited joint mobility is associated with flexor tenosynovitis (Benedetti et al. 1982; Chammas et al. 1995; Griggs et al. 1995; Ismail et al. 1996; Kameyama et al. 2009; Pincelli et al. 1997; Sibbitt & Eaton 1997), Dupuytren's disease (Pal et al. 1987), carpal tunnel syndrome (Chaudhuri, Davidson & Morris 1989) and frozen shoulder (Pal et al. 1986). Careful examination to differentiate these conditions is required as pain, stiffness, loss of fine movements, reduced grip strength or clumsiness may be presenting complaints that interfere with daily tasks, including difficulties in using insulin syringes (Pal 2003).

1.4.3 PROPOSED AETIOLOGICAL MECHANISMS

The inter-relationships of limited joint mobility with these other hand syndromes, and an association with the microvascular complication of retinopathy, may be explained by the duration of diabetes (Campbell et al. 1985; Fernando & Vernidharan 1997; Pal et al. 1986), by sharing similar aetiological mechanisms (Kapoor & Sibbitt 1989; Rosenbloom et al. 1981; Sibbitt & Eaton 1997) or be related to an individual's genetic susceptibility (Brice, Johnston & Noronha 1982).

The proposed aetiological mechanisms underlying connective tissue changes in response to diabetic hyperglycaemia, represented in figure 1.3, include:

- Increased flux through the polyol pathway. An important part of the polyol pathway is the actions of the enzyme, aldose reductase. When glucose concentrations are increased in cells, the enzyme aldose reductase increases the breakdown of glucose to sorbitol, which is subsequently oxidised to fructose. This process increases intracellular oxidative stress (Brownlee 2005). The accumulation of sorbitol in cells may also cause swelling by creating an osmotic gradient that increases the movement of water into cells (Kapoor & Sibbitt 1989). Eaton, Sibbitt and Harsh (1985) have also proposed that, in addition, increased hydration of collagen could contribute to the finger oedema and joint stiffening seen in limited joint mobility.
- Increased formation of advanced glycosylation endpoints. Persistent hyperglycaemia induces excessive glycosylation of proteins, including collagen. Glycosylated collagen has quite stable crosslinks that make it resistant to enzymatic and chemical breakdown. The increased crosslinking of glycosylated collagen increases its strength and reduces its turnover (Buckingham et al. 1984). The accumulation of glycosylated collagen may be responsible for the periarticular and skin thickening seen in limited joint mobility (Arkkila & Gautier 2003; Collier et al. 1986; Lyons & Kennedy 1985).
- Increased free-radical-mediated oxidative damage to lipids and proteins, may also contribute to the development of connective tissue changes in the hand in diabetes. Free radical reactions may in themselves generate crosslinks in proteins, and thus the changes in collagen in may be the result of increases in glycosylation, non-enzymatic browning and oxidation reactions (Lyons & Kennedy 1985)

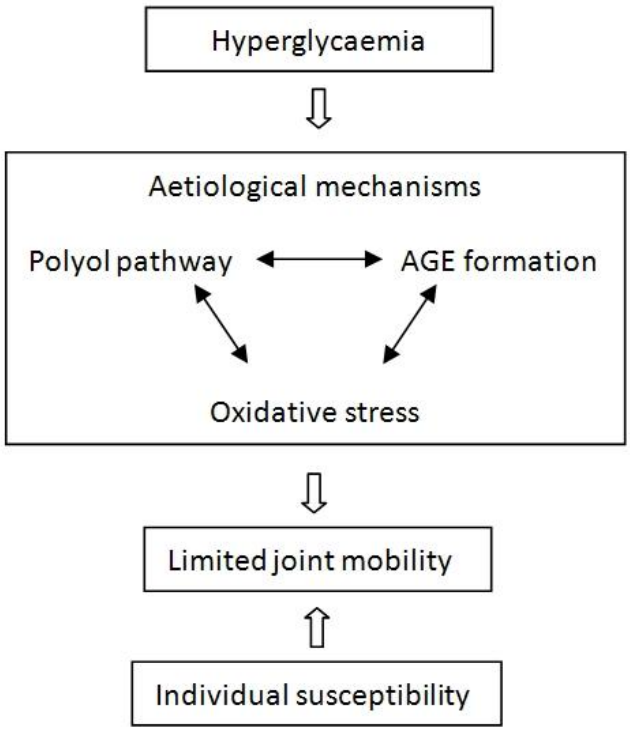

Figure 1.3 Proposed mechanisms underlying the connective tissue changes in the syndrome of limited joint mobility.

AGE = advanced glycosylation endpoint

1.4.4 TREATMENT

The treatment of limited joint mobility requires further investigation. Recommendations requiring further evidence include improving control of hyperglycaemia (Kapoor & Sibbitt 1989; Lister, Graham-Brown & Burden 1986) and physiotherapy to regain finger mobility (Aljahlan, Lee & Toth 1999; Kapoor & Sibbitt 1989; Smith, Burnet & McNeil 2003).

Pharmacological therapy to influence collagen metabolism has been investigated. A positive response to treatment by an aldose reductase inhibiting agent was reported in three cases (Eaton, Sibbitt & Harsh 1985) but a small randomised clinical trial showed no benefit in the management of limited joint mobility (Rosenbloom et al. 1992). Potentially adverse side effects are a concern with this therapy (Aljahlan, Lee & Toth 1999).

Treatment has been directed to the associated flexor tenosynovitis or triggering of fingers. Corticosteroid injection into the tendon sheath of affected fingers has

improved finger mobility and reduced triggering (Sibbitt & Eaton 1997) and a case of tenolysis, or operative freeing of a tendon from adhesions, has also been reported (Robertson, Earnshaw & Campbell 1979).

1.5 Carpal tunnel syndrome

Carpal tunnel syndrome is the most common entrapment neuropathy affecting the upper limb. In the general population, it is estimated to occur in 3% of women and 1% of men. But in diabetes, the prevalence of carpal tunnel syndrome is estimated to range from 6 to 30% (Chammas et al. 1995; Perkins, Olaleye & Bril 2002; Renard et al. 1994) and occurs more frequently in type 1 diabetes (Cagliero et al. 2002; Dyck et al. 1993; Gamstedt et al. 1993; Renard et al. 1994). In diabetes, bilateral presentations (Becker et al. 2002) or gradual onset affecting the dominant hand (Fraser et al. 1979) have been described.

1.5.1 PROPOSED AETIOLOGICAL MECHANISMS

The relatively inelastic structure of the carpal tunnel makes the median nerve at risk of compression if pressure in the tunnel is increased. Many factors influence pressure within the carpal tunnel and are implicated in the development of carpal tunnel syndrome. Trigger finger or flexor tenosynovitis are common concurrent presentations suggesting that synovial thickening and oedema of the tendon sheaths increase pressure within the carpal tunnel (Kumar & Chakrabarti 2009; Neal, McManners & Stirling 1987; von Schroeder & Botte 1996). Ergonomic stresses related to work have been implicated (Gell et al. 2005) and conditions or diseases that increase inflammation or oedema within the carpal tunnel, or predispose to peripheral neuropathy have also associated with carpal tunnel syndrome (Solomon et al. 1999; Sternbach 1999).

1.5.2 CONTRIBUTING FACTORS IN DIABETES

The factors that contribute to the increased prevalence of carpal tunnel syndrome in diabetes remain uncertain. The median nerve may be more susceptible to daily mechanical stresses and compression if it has been subjected to prior ischaemia (Fraser et al. 1979), when distal symmetrical neuropathy is present (Perkins, Olaleye & Bril 2002) or when trigger finger or the syndrome of limited joint

mobility are present (Chaudhuri, Davidson & Morris 1989; Rottgers, Lewis & Wollstein 2009).

Changes in cellular metabolism in response to hyperglycaemia can result in peripheral nerve ischemia and increase the susceptibility to compression. In addition, neuronal plasticity is compromised in diabetes, resulting in less capacity to recover from these damaging effects (Kennedy & Zochodne 2005; Ozkul et al. 2002; Solomon et al. 1999).

Obesity often precedes type 2 diabetes and it is difficult to separate its contribution to carpal tunnel syndrome. Obesity has been implicated as contributing to carpal tunnel syndrome (Becker et al. 2002; Bland 2005; Lam & Thurston 1998; Nathan, Istvan & Meadows 2005; Werner, Jacobson & Jamadar 2004), as well as the metabolic syndrome of abdominal obesity, dyslipidemia, hyperglycaemia and hypertension (Balci & Utku 2007). It has been suggested that obesity increases hydrostatic pressure within the carpal tunnel, and subsequent compression of the median nerve (Becker et al. 2002) or that abnormal glucose metabolism occurring in obesity contributes to neural oedema and subsequent slowing of median nerve conduction (Gulliford et al. 2006; Werner, Jacobson & Jamadar 2004).

1.5.3 NERVE CONDUCTION STUDIES

The most accurate diagnosis of carpal tunnel syndrome is from characteristic symptoms in conjunction with nerve conduction abnormalities (Rempel et al. 1998). However, clinical examination should guide the diagnosis. Abnormal slowing of nerve conduction velocities is detected frequently in diabetes, may affect both the median and ulnar nerves, be difficult to distinguish from peripheral neuropathy and may not be associated with typical symptoms of carpal tunnel syndrome (Imada et al. 2007; Stamboulis et al. 2009).

1.5.4 TREATMENT OPTIONS

Current recommendations for the treatment of carpal tunnel syndrome include trialling non-operative treatments when the diagnosis of carpal tunnel syndrome is made, as well as the surgical option of carpal tunnel release. There is moderate evidence for the efficacy of the non-operative treatments of wrist splinting,

ultrasound and injection of corticosteroids into the carpal tunnel in idiopathic carpal tunnel syndrome (Keith et al. 2010) but splinting has been an ineffective treatment in diabetes (Kiylioglu et al. 2009).

There is strong evidence for the success of carpal tunnel release in idiopathic carpal tunnel syndrome (Keith et al. 2010) but less evidence for its efficacy in diabetes. Carpal tunnel release has been effective in diabetes (Haupt et al. 1993; Mondelli et al. 2004; Ozkul et al. 2002; Thomsen et al. 2009), although there may be differences in relief of symptoms and recovery of nerve conduction velocities (Haupt et al. 1993; Ozkul et al. 2002). The results of carpal tunnel release when peripheral neuropathy is present are somewhat contradictory. Surgical release has been effective when diabetic peripheral neuropathy is present (Thomsen, Rosen & Dahlin 2010), but it was postulated that it contributed to the 25% of poor results in a retrospective review of cases (al-Qattan, Manktelow & Bowen 1994). A recent study has also investigated infection rates after carpal tunnel release and found no significant difference for those with diabetes (Harness et al. 2010).

However, other features of the presentation, such as trigger finger or severe obesity (BMI > 35), may reduce the success of treatment (Bodavula et al. 2007; Kaplan, Glickel & Eaton 1990). Adjunctive procedures to carpal tunnel release, such as tenosynovectomy, have not been investigated in diabetes but it has been recommended that to improve results from carpal tunnel release, treatment extend to managing poorly controlled diabetes and obesity (Arkkila & Gautier 2003; Ozkul et al. 2002).

1.6 Trigger finger

Trigger finger, or stenosing tenosynovitis, presents with catching or locking that may be painful, when the finger is flexed or extended. The onset is usually gradual with intermittent symptoms that may be worse in the morning. The gliding of the flexor tendon is usually obstructed at the level of the A1 pulley, a component of the flexor tendon sheath. This obstruction may ultimately block movement and so the finger locks on flexion. In conjunction with the characteristic symptoms, tenderness or thickening of the soft tissues may be detected, when the palm is palpated at the level of the A1 pulley (Moore 2000).

Trigger finger is more common in diabetes (Chammas et al. 1995; Yosipovitch et al. 1990). Multiple fingers may be affected (Blyth & Ross 1996; Griggs et al. 1995; Stahl, Kanter & Karnielli 1997) and both hands involved (Blyth & Ross 1996).

1.6.1 PROPOSED AETIOLOGICAL MECHANISMS

While the mechanisms behind the increased prevalence in diabetes is uncertain, it is proposed that thickening and stiffening of the flexor tendon sheath (Stahl, Kanter & Karnielli 1997) or enlargement of the flexor tendons (Marcus, Culver & Hunt 2007) occurs, following non-enzymatic glycosylation of collagen.

1.6.2 TREATMENT OPTIONS

Management strategies include modifying activities to reduce frictional forces at the A1 pulley from repetitive gripping or compression, applying splinting in metacarpal extension to avoid increased forces from end of range finger flexion or injecting corticosteroid into the flexor tendon sheath to reduce inflammation (Moore 2000). Surgical options to improve tendon excursion include release of the A1 pulley (Ryzewicz & Wolf 2006), tenosynovectomy and excision of the ulnar slip of the flexor digitorum superficialis (Marcus, Culver & Hunt 2007).

However, trigger finger is less responsive to treatment in diabetes (table 1.2). Steroid injection is less effective (Baumgarten, Gerlach & Boyer 2007; Stahl, Kanter & Karnielli 1997), particularly in those with type 1 diabetes (Griggs et al. 1995; Rozental, Zurakowski & Blazar 2008) and physiotherapy may be required to manage post-operative stiffness or pain (Stahl, Kanter & Karnielli 1997). Multiple trigger digits (Rozental, Zurakowski & Blazar 2008), poor control of diabetes or the presence of other diabetic complications (Baumgarten, Gerlach & Boyer 2007) are factors that have indicated a poorer response to injection.

Table 1.2 Rates of symptoms recurring in those with and without diabetes treated for trigger finger

DM = diabetes mellitus

AUTHOR, YEAR	SAMPLE	FOLLOW-UP (MONTHS)	TREATMENT	RECURRENCE (%)
Rozental (2008)	119 patients (20 DM2, 6 DM1)	12	injection	56%;100% DM1
Baumgarten (2007)	30 DM; 29 control	12	injection	14% controls; 37% DM
Sibbitt (1997)	15 diabetes	12	injection	39% DM
Stahl (1997)	60 DM, 60 control	4	injection	24% controls; 51% DM
			surgery	6% controls; 23% DM
Griggs (1995)	54 DM	?	injection	50 % DM
			surgery	9% DM

Patients should be advised that recurrence rates following injection are high and symptoms can occur within months (Rozental, Zurakowski & Blazar 2008). Blood glucose levels may also be temporarily elevated, particularly in type 1 diabetes (Wang & Hutchinson 2006). Despite these disadvantages, complications are rare and so it remains an initial treatment option (Baumgarten 2008). Given the high rates of recurrence, however, some patients might choose to wait and see if spontaneous resolution occurs or opt for pre-emptive surgery.

1.7 Atypical Dupuytren's disease

Dupuytren's disease causes thickening or contracture of the palmar fascia. It is diagnosed from observing one or more of four characteristic features (McGrouther 1990; Noble, Heathcote & Cohen 1984)

- a palpable nodule in the palmar or digital fascia
- tethering of the skin causing distortion of the palmar creases, dimpling of the skin or blanching on full finger extension
- development of thickened cords and bands that extend to the digital fascia
- finger joint contracture

The presentation of Dupuytren's disease in diabetes is atypical (table 1.3). It is likely to be a separate clinical identity with a different prognosis (Fitzgibbons & Weiss 2008; Rayan & Moore 2005).

Table 1.3 Dupuytren's disease features in those with and without diabetes.

DUPUYTREN'S DISEASE	DUPUYTREN'S DISEASE IN DIABETES
Predominantly affects men	Men and women equally affected
Little or ring fingers usually involved	Middle or ring fingers usually involved
Progression and recurrence common in diathesis	Progressive contractures are rare

Dupuytren's diathesis:
• Family history
• Ethnic background
• Bilateral presentation
• Ectopic fibromatosis:
  • knuckles (Garrod's pads)
  • penis (Peyronie's disease)
  • plantar fascia (Lederhose's nodules)
	Nodules are common
	Plantar fibromatosis are uncommon (Lederhose's nodules)

In the general population, Dupuytren's disease has a strong family tendency, a "Dupuytren's diathesis" has been described, men are predominantly affected and the little and ring fingers are commonly involved (Gudmundsson et al. 2000; Hindocha et al. 2006). In diabetes, however, women are equally affected, the

middle and ring fingers are commonly involved, progressive contractures are rare (Chammas et al. 1995; Noble, Heathcote & Cohen 1984; Rayan & Moore 2005) (figures 4 and 5) and while plantar fibromatosis has been reported (Elhadd et al. 2007; Reilly, Stern & Goldfarb 2005), the assessment of fibromatosis at other sites has tended to be overlooked.

Structural differences in the contracted bands of palmar fascia from individuals with diabetes also suggest that it is a different clinical syndrome. The bands consisted of fibril bundles, formed by cross linking of adjacent collagen fibrils that indicated advanced glycation endpoint formation. In contrast the contracted bands in those without diabetes, had increased type III collagen, loss of fascicular organisation and reduced cross linking that suggested a different pathology (Melling et al. 1999).

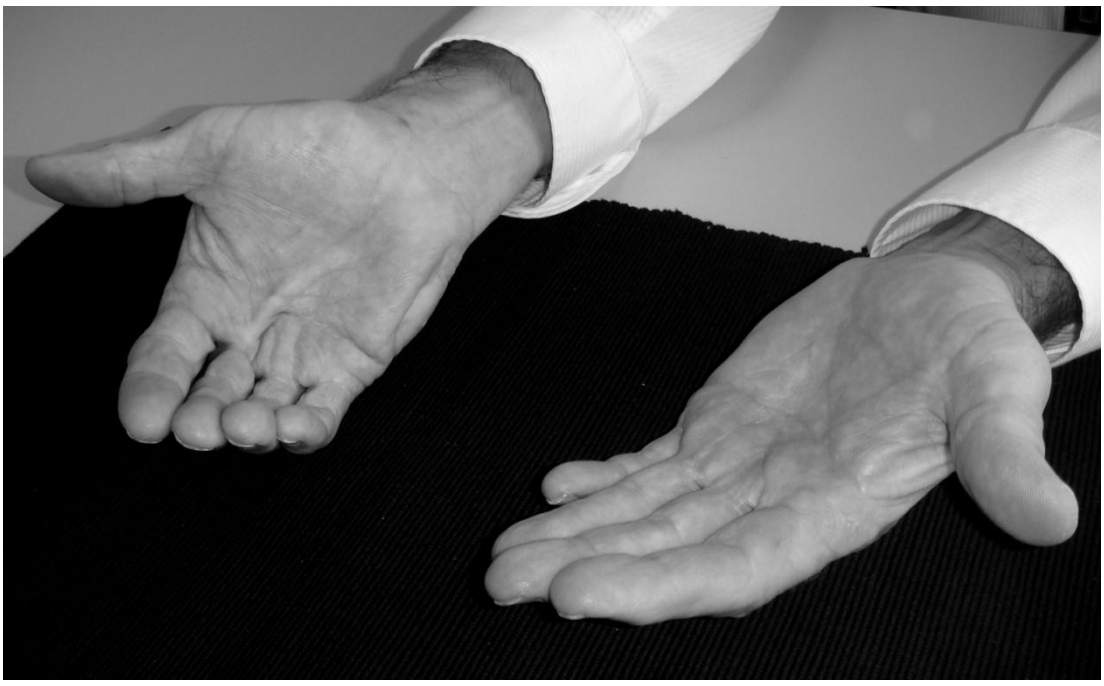

Figure 1.4 Prominent Dupuytren's cord in line with the right middle finger.

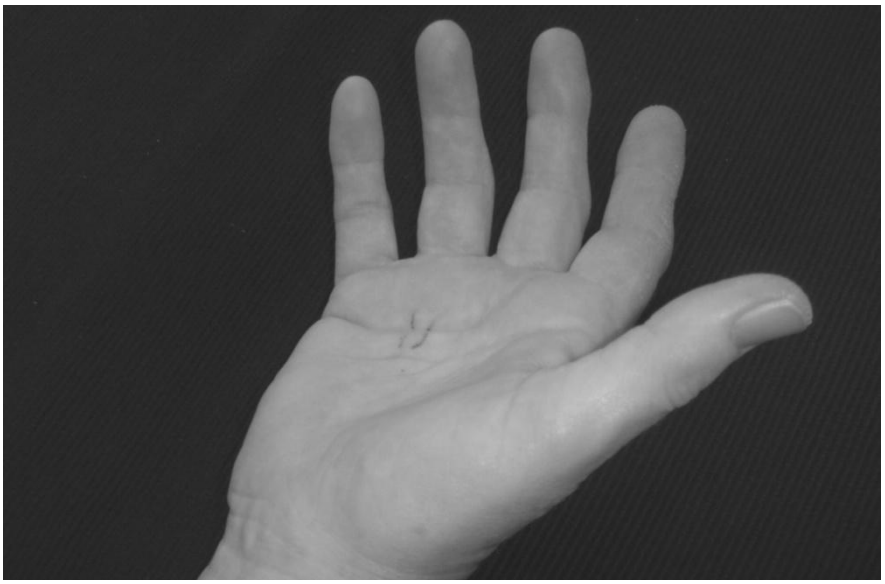

Figure 1.5 Dupuytren's nodule in line with the right ring finger
The nodule was outlined on the hand for visibility

1.7.1 ASSOCIATED FEATURES

Atypical Dupuytren's disease in diabetes is associated with older age and longer duration of diabetes (Arkkila, Kantola & Viikari 1997; Heathcote, Cohen & Noble 1981; Pal et al. 1987), with retinopathy (Larkin & Frier 1986; Lawson, Maneschi & Kohner 1983; Pal et al. 1987), with nephropathy in type 2 diabetes (Arkkila, Kantola & Viikari 1997) and with microalbuminuria, an early sign of nephropathy in type 1 diabetes (Montana et al. 1995).

1.7.2 TREATMENT OPTIONS

Surgical management by fasciectomy to regain finger extension is an option for Dupuytren's disease if finger contracture is progressing and functional difficulties are occurring. Percutaneous needle fasciotomy to divide a cord is an alternative and simpler treatment in selected cases (Foucher, Medina & Navarro 2003). The recovery period after fasciectomy can be long and rates of recurrence are high (Trojian & Chu 2007), with some evidence that recurrence after surgery occurs more frequently in diabetes (Norotte, Apoil & Travers 1988). The development of limited joint mobility as a post-operative complication has also been reported in diabetes (Fournier et al. 2008).

1.8 Summary

- The high prevalence of hand disorders in diabetes is well established.
- Distinctive patterns of presenting signs and symptoms are recognised for these disorders.
- Relationships with other upper limb disorders and with micro-vascular complications of diabetes have been determined.
- Obesity is implicated as a risk factor for developing carpal tunnel syndrome.
- Hand disorders occur more frequently in longstanding diabetes but the relationship with diabetes control is uncertain.
- Longstanding diabetes is associated with muscle weakness and physical limitations.
- Studies investigating the results of managing these disorders have found poorer outcomes when treating trigger finger and carpal tunnel syndrome in those with diabetes.

1.9 Rationale for the study

Objective documentation of levels of hand disability, associated impairments and health-related quality of life may identify clinical patterns associated with hand disability. This is important for identifying individuals who may be at risk of developing disability or have poorer outcomes to current management strategies; or may be used to develop new directions for management.

This study was designed to answer these questions:

- To what extent are adults with diabetes functionally limited by these hand syndromes?
- Are impairments of strength and tactile sensation associated with these hand syndromes and related to functional limitations?
- Are personal factors, such as age, gender or a person's health-related quality of life associated with limited hand function?
- Are factors related to diabetes, such as obesity, the duration since diagnosis, diabetes type or control associated with limited hand function?

The longitudinal study was designed to answer the additional question:

- At what rate do different aspects of hand function change over time?

1.10 Aims

In a sample of adults with diabetes-associated hand disorders:

- To characterise their hand function and health-related quality of life
- To measure the associated impairments of strength and tactile sensation
- To identify factors associated with poorer hand function
- To evaluate changes in hand function over annual reassessments

1.11 Hypotheses

Adults with diabetes-associated hand disorders will:

- Have decreased hand function compared to population norms
- Have poorer health-related quality of life compared to population norms
- Have greater impairments compared to population norms
- Aspects of hand function will deteriorate with time, over successive assessment

CHAPTER 2. MEASURING HAND FUNCTION

2.1 Introduction

Assessing hand function is an integral part of managing hand disorders as it is a part of recognising individual variations in presentations, it determines which treatment options are effective and distinguishes individual responses to treatment. Hand assessments may cover different aspects of symptoms, physiological impairments, the impact on activities of daily living or other factors that affect individual functioning and clinicians need to decide which assessments will be the most appropriate and sensitive in detecting change (Clarke, AE & Fries 1992; Rudman & Hannah 1998).

This process is influenced by the development of new instruments and changing standards in evaluating health outcomes. There has been a shift from assessing physical measures of impairment to assessing self-reported measures of the ability to function. This shift incorporates the patient's perspective, and hence focuses on concerns about symptoms and the ability of an individual to perform activities required in daily life; and also reflects concerns about inconsistent relationships between measures of impairment and functional abilities (Dekkers & Soballe 2004; Hobby, Watts & Elliot 2005; Jerosch-Herold 1993; Levine et al. 1993).

Incorporating the patient's perspective is in line with the World Health Organisation (WHO) model of health, which proposes that the consequences of disease impacts health sequentially across the three dimensions of bodily structures and functions, activities and participation (World Health Organisation 2001). Physical assessments of aspects such as muscle strength, sensation or range of movement are measuring bodily structures and functions. The other dimensions of the performance of activities required in daily life, and participation in work and leisure, are usually self-reported. All dimensions can be influenced by environmental and personal factors. The negative aspect of developing disability is described across the dimensions as impairment, activity limitation and participation restriction.

Designing a comprehensive assessment is not straightforward. The hand assessment needed to be standardised for group comparisons and assess the most relevant physiological impairments in order to evaluate the relationships between

impairments and limitations of activities. Furthermore, deciding which instruments best measure these aspects can also be complex. From the many instruments and methods available for clinical use, instruments were selected with evidence of acceptable reliability and validity so that accurate comparisons could be performed over successive assessments.

2.2 Rationale

The assessment was designed to evaluate the hands clinically and assess health more broadly. It was standardised for group comparisons and decisions were made as to which physiological impairments were most relevant to assess in diabetes.

2.3 Selected instruments

The key components of the hand assessment were to measure the impact of the hand disorders on daily work or other activities, physiological impairments that might be impacting on activities and the psychosocial consequences of these limitations.

The selected instruments were:

- Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire
- Short-Form 36-item Health Survey, version 2 (SF-36v2)
- Dynamometer measurement of grip strength
- WEST monofilaments measurement of light touch perception
- 9-hole peg test of capacity for dexterity

Two self-reported measures were selected. The DASH measures symptoms and upper limb function and was suitable in those with bilateral presentations, or with coexisting conditions affecting other upper limb joints. The SF-36v2, a generic health status measure, was selected to more broadly measure the psychosocial impacts of these hand disorders in diabetes. These two self-reported measures could give complimentary but distinct pictures of health (Bombardier et al. 1995). Grip strength, sensory function and fine motor skills were selected as being potentially related to hand disability in this population. Measuring these physiological impairments and limitations in abilities could identify potential

treatment options, which in turn, could have implications for improving patient care.

2.4 Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire

2.4.1 DESCRIPTION

The Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire was developed to assess symptoms and functional status, with a focus on physical function, in populations with upper limb musculoskeletal conditions (Hudak et al. 1996). In contrast to other disease or joint specific questionnaires it was designed to permit comparison across various groups of patients or treatments. The concept that the upper limb worked as a functional unit underpinned the development of a questionnaire for the upper limb rather than, for example, more specifically for the shoulder joint or for carpal tunnel syndrome (Davis, AM et al. 1999).

It has 30 items with each item having five response options and takes from five (Bot et al. 2004) to 15 minutes to complete (Changulani et al. 2008). The items ask about the degree of difficulty performing everyday activities in the previous week (21 items), the effect of the upper limb problem on social activities, work or daily activities, sleep and emotional health (4 items), and symptoms of pain, tingling, weakness or stiffness (5 items). It is scored on a scale from 0 to 100, where higher scores indicate increasing symptoms and functional difficulties. At least 27 items need to be completed for a valid score to be generated.

$$\text{The DASH score} = [(\text{sum of n responses}/n) - 1] \times 25,$$

where n is the number of completed responses.

2.4.2 RELIABILITY, VALIDITY AND SENSITIVITY TO CHANGE

The DASH has had high test-retest reliability (ICC = 0.96, Cronbach alpha coefficient > 0.9) (Beaton, Katz, et al. 2001; Gummesson, Atroshi & Ekdahl 2003). It has demonstrated construct validity with the Brigham carpal tunnel questionnaire (Beaton, Katz, et al. 2001) and with moderate correlations with the SF-36 scales (SooHoo et al. 2002). The questionnaire's sensitivity to change, which is reported by effect sizes or standardized response means, has varied

substantially depending on the situation and the type of change being examined. The DASH has been responsive to improvement before and after treatment for a variety of surgical or therapeutic procedures including carpal tunnel release and hand therapy (ES, 0.7 to 1.59, SRM, 0.66 to 1.76) (Greenslade et al. 2004; Gummesson, Atroshi & Ekdahl 2003; MacDermid, J C & Tottenham 2004). The minimal detectable change (MDC), or the amount of change required to exceed measurement error, has been calculated as 11(MacDermid, J C et al. 2007) and 12.75 points (Beaton, Katz, et al. 2001). A different estimate of change, the clinically important difference (CID), incorporated self-reported improvement in its calculation and has been estimated as 10 points (95% CI, 7 to 14 points) (Gummesson, Atroshi & Ekdahl 2003).

2.5 Short-Form 36-item Health Survey, version 2 (SF-36v2)

2.5.1 DESCRIPTION

The Short-Form 36-item Health Survey, version 2 (SF-36v2), was developed by the Medical Outcomes Trust in the United States and is the most widely used generic health survey. Generic questionnaires aim to cover multiple aspects of health and quality of life of relevance to the individual and to the general population (Guyatt, Feeny & Patrick 1993). SF-36v2 was developed after ten years of use of the original version and incorporated slight modifications in wording and layout. It measures attributes of health across eight separate scales that can be collapsed to a physical and a mental health summary scale.

The scales are:

- Physical Function (10 items)
- Role Physical (2 items)
- Bodily Pain (2 items)
- General Health (5 items)
- Vitality (4 items)
- Social Functioning (2 items)
- Role Emotional (3 items)
- Mental Health (5 items)

Although widely used in research, the SF-36v2 is less accepted in clinical practice as it is impractical to score by hand. Scores are calculated in four steps:

- responses to ten items are recoded
- responses in the same scales are summed to generate raw scale scores
- raw scale scores are transformed to scores on a scale from zero to 100
- transformed scores are transformed again to have a mean of 50 and a standard deviation of 10 in the general US population

An additional question on changes in health in the previous year is not included in the final score. Scores are transformed to US population norms so observed scores for the different scales can be interpreted in relation to population averages (Ware, Kosinski & Dewey 2000). The instrument has been successfully adapted for use in a number of countries, including an authorised Australian version.

2.5.2 RELIABILITY, VALIDITY AND SENSITIVITY TO CHANGE

The validity and reliability of the SF-36v2 is well established as an instrument able to discriminate between individuals with a range of medical conditions with varying levels of severity (McCallum 1995; McHorney et al. 1994). It has been validated in populations with musculoskeletal conditions and it has been found that the scales measuring physical health best distinguished the presence and severity of musculoskeletal complaints (Liang, Fossel & Larson 1990). In the diabetic population, poor control of blood glucose levels as well as the strict regimens for tight control in DM1 has reduced well-being and quality of life (Nerenz et al. 1992).

As a generic questionnaire, it has the advantages of measuring health status broadly and focussing attention on issues of quality of life of importance to the patient. It can provide a comparison of health status data across different patient groups. However, it also has the disadvantage of being less responsive to clinical change in hand and wrist disorders than more specific questionnaires (Amadio et al. 1996; Bessette et al. 1998; Katz et al. 1998).

2.6 Grip strength

2.6.1 DESCRIPTION

Grip strength was assessed using the dynamometer attachment of the Eval® Hand Evaluation System (Greenleaf Medical Systems, Palo Alto, CA). The Eval® electrodynamometer is based on the design of the Jamar dynamometer but an electronic sensor has replaced the analog gauge. It measures static grip in pounds or kilograms of force.

Although grip strength can be measured across five handle positions, the second handle position was selected as this handle position generally produces the strongest grip strength (Crosby, Wehbe & Mawr 1994; Harkonen, Piirtomaa & Alaranta 1993) and it is recommended in standardised procedures (Casanova 1992).

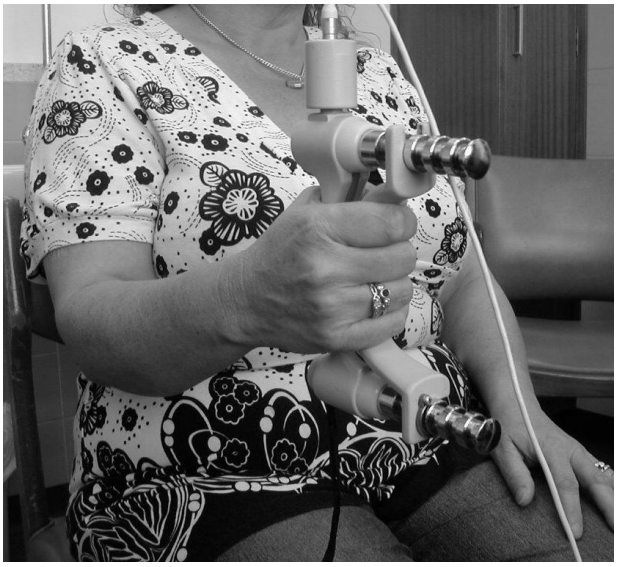

Figure 2.1 Grip strength was assessed with the Eval® electrodynamometer using the second handle position

2.6.2 RELIABILITY, VALIDITY AND SENSITIVITY TO CHANGE

It was assumed that, with acceptable calibration, the Eval® dynamometer would perform in the same way as the Jamar dynamometer because of similarities in its design. The Jamar dynamometer has very good intra-observer reliability and excellent inter-observer reliability using standardised methods and instructions in healthy subjects (Hamilton, Balnave & Adams 1994; Mathiowetz, Kashman, et al. 1985). Dynamometers have reliably measured grip strength in individuals with

various clinical conditions (Lagerstrom, Nordgren & Olerud 1999; MacDermid, J C et al. 1994) but have been less reliable in those with chronic pain (Harding et al. 1994). Periodically assessing the calibration of all dynamometers to ensure that they remain accurate and reliable over time is a general recommendation (Fess 1995). The factory calibration of the Eval® electrodynamometer was verified using known weights suspended from the handle.

The minimal detectable change (MDC), or the amount of change required to exceed measurement error, has been calculated with 95% confidence as 6kg (Nitschke et al. 1999)

2.6.3 INFLUENCES ON GRIP STRENGTH

Grip strength is a measure the strength of the hand but has also been shown to correlate well with total body strength (Davis, JW et al. 1998; Syddall et al. 2003). It varies over a lifespan and is influenced by a number of factors. There is a curvilinear relationship with age, so that generally grip strength rises to a peak when an individual is aged in their thirties or early forties and thereafter gradually declines as aging affects muscle mass and quality (Desrosiers et al. 1995; Hanten et al. 1999; Kallman, Plato & Tobin 1990)

One of the strongest predictors of lower grip strength is female gender and while physical training in women can significantly increase grip strength it usually remains lower compared to men (Leyk et al. 2007). Other predictors include hand dominance, lower body height, being underweight or obese, recreational choices, difficulties with functional tasks and the presence of co-morbidities (Crosby, Wehbe & Mawr 1994; Forrest, Zmuda & Cauley 2007; Harkonen, Piirtomaa & Alaranta 1993; Kellor et al. 1971; Massy-Westropp, N et al. 2004; Mathiowetz, Kashman, et al. 1985; Petersen et al. 1989). An additional source of some variation is normal fluctuation of individual strength (Young, VL et al. 1989). Understanding factors influencing lower grip strength is important for developing strategies to strengthen the hand and improve function.

2.6.4 CALIBRATION STUDY OF EVAL® DYNAMOMETER

The Eval® dynamometer, when originally purchased, was factory calibrated to an accuracy of better than 1.0 percent.

To check the calibration, the dynamometer was supported on the level between two benches. A strap was placed over the grip from which known weights could be suspended. Calibrated weights were added in increments so an increasingly heavier total weight was suspended from the strap and then were gradually removed so the total weight gradually decreased again. The instrument readout of the increments and decrements in weight was recorded (table 2.1). A slight lag in response to changes in weight, known as a hysteresis effect, was noted. The performance of the dynamometer at the lightest weight (1.1kg) was also noticed to be worse. Percentage errors were calculated. The Pearson r correlation coefficient between the suspended weights and the dynamometer readout was calculated as a measure of accuracy.

The average error was 2.2%. An average error of up to 3% is considered acceptable (Fess 1987; Harkonen, Harju & Alaranta 1993), so the Eval® dynamometer correlated with acceptable accuracy with the suspended weight (r = 0.9997).

Table 2.1 Percentage differences were calculated by comparing the total of the standardised weights to the Eval® dynamometer readout.

Standard weight (kg)	Total (kg)	Eval® readout	Difference (%)
1.1	1.1	1	9.09
5.1	6.2	6	3.23
5.1	11.3	11	2.65
4.54	15.84	16	1.01
4.52	20.36	20	1.77
4.08	24.44	24	1.80
2.26	26.7	26	2.62
3.182	29.882	29	2.95
2.727	32.609	31	4.93
-2.727	29.882	29	2.95
-3.182	26.7	27	1.12
-2.26	24.44	24	1.80
-4.08	20.36	20	1.77
-4.52	15.84	16	1.01
-4.54	11.3	11	2.65
-5.1	6.2	6	3.23
-5.1	1.1	1	9.09
-1.1	0	0	0.00
35.38	35.38	35	1.07
4.52	39.9	40	0.25
4.08	43.98	43	2.23
2.26	46.24	45	2.68
3.182	49.422	49	0.85
2.727	52.149	51	2.20
-2.727	49.422	49	0.85
-3.182	46.24	46	0.52
-2.26	43.98	44	0.05
-4.08	39.9	40	0.25
-4.52	35.38	35	1.07
-19.54	15.84	16	1.01
-15.84	0	0	
		% diff (mean)	**2.2**

2.6.5 RELATIONSHIPS WITH PHYSICAL FUNCTIONING

As a simple measure of muscle function grip strength has been used in clinical and population studies to assess relationships with functional abilities and participation. Grip strength is often used as an outcome measure for musculoskeletal conditions. For carpal tunnel syndrome, decreased grip strength has been related to greater functional difficulties (Hobby, Watts & Elliot 2005) but it has not been the most sensitive measure of change in the short term following carpal tunnel release (Amadio et al. 1996; Geere et al. 2007; Olsen & Knudson 2001).

Declines in skeletal muscle mass occur in older adults to varying degrees and can be influenced by multiple factors, including hormonal changes, inactivity, disease and poor nutrition. Grip strength may be a marker for this loss in muscle mass, which is reflected in its correlation with work capacity (MacDermid, J C, Roth & Richards 2003), old age disability (Giampaoli et al. 1999; Rantanen et al. 1999), health status and quality of life (Sayer et al. 2006).

2.6.6 PROTOCOL

The participants were tested while sitting using standardised positioning and verbal directions (Mathiowetz, Kashman, et al. 1985). Following a demonstration, each participant was given a practice trial for each hand.

Three trials of maximal static grip were performed. The measurements started with the dominant hand and alternated between hands. The maximal grip strength in kilograms of force was calculated as the average of the three trials for each hand.

2.7 Sensory perception

2.7.1 DESCRIPTION

The sensory status of the peripheral nerves was assessed with the Weinstein Enhanced Sensory Test (WEST) set of five monofilaments for testing the hand. This test evaluates an individual's perception of a stimulus applied to the skin. Monofilaments of gradually increasing stiffness are applied to the skin in a controlled manner in order to determine the lightest force, or the threshold, that is felt by an individual (figure 2.3).

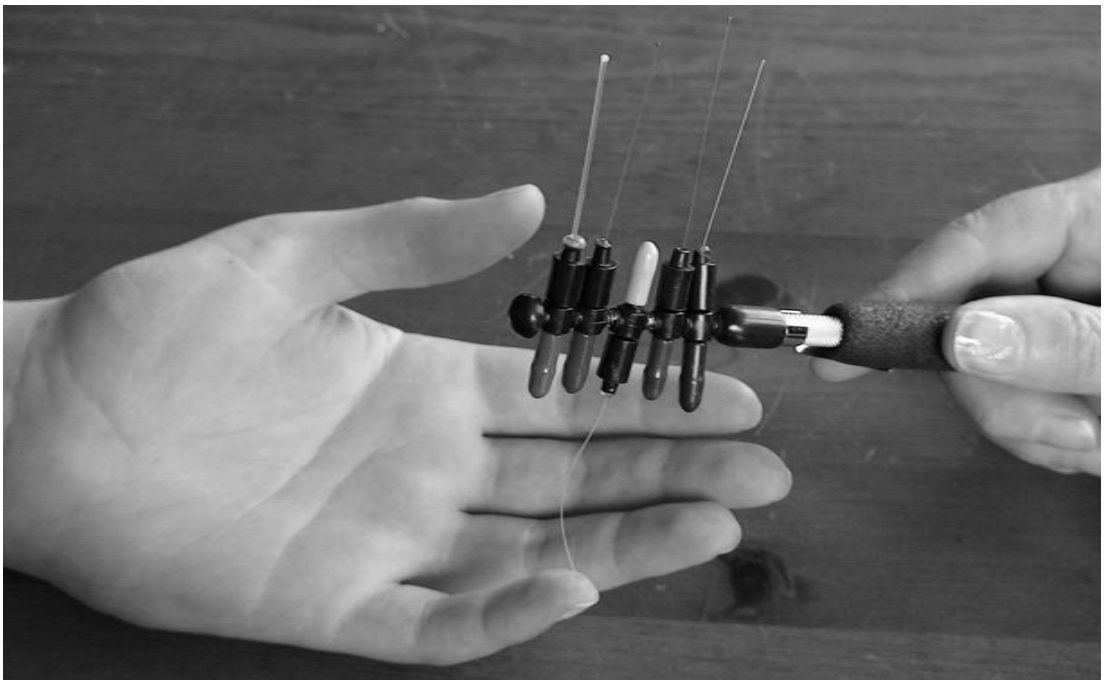

Figure 2.2 Light touch perception was assessed with WEST monofilaments at specific sites on the hand

There are many tests that evaluate sensory perception of pain, vibration, temperature, two-point discrimination, touch and pressure thresholds (Casanova 1992; Waylett-Rendall 1988). However, testing touch and pressure perception with monofilaments has advantages of being one of the most reliable tests for acute compression (Gelberman et al. 1983) and more sensitive than two-point discrimination in chronic compression neuropathies (Szabo, R M, Gelberman & Dimick 1984).

The WEST set was developed from the Semmes Weinstein set of 20 monofilaments. The design of the monofilament tip was improved by making it more rounded, to more specifically stimulate light touch and help prevent slippage. Factory calibration has been incorporated to improve reliability. The five monofilaments in the WEST set were selected as being most predictive of changes in functional status. They represent the cut-off forces for normal sensation; diminished light touch; diminished protective sensation; loss of protective sensation and basic deep-pressure sensation (Bell-Krotoski 1995) (table 2.2).

Table 2.2 The values, applied force and functional status for the WEST hand set of monofilaments

Monofilament value	Applied force (grams)	Functional status
5	0.07	Normal sensation
4	0.2	diminished light touch
3	2	diminished protective sensation
2	4	loss of protective sensation
1	200	basic deep-pressure sensation

2.7.2 RELIABILITY, VALIDITY AND SENSITIVITY TO CHANGE

Monofilaments have acceptable intra-observer reliability because they bend consistently as peak-force threshold is achieved. Generally, reliability has been tested using Semmes-Weinstein monofilaments but the WEST should have similar reliability, as the two instruments have demonstrated a correlation of 0.99 in detecting the same thresholds (Weinstein 1993).

The same examiner should conduct successive tests as inter-observer reliability has varied, sometimes unacceptably (Bowen, Griener & Jones 1990; MacDermid, J C, Kramer & Roth 1994; Marx et al. 1998; Massy-Westropp, N. 2002). It may be that different observers interpret responses differently or develop differences in their methods of application that influence individual responses. While the reason behind differences between observers is uncertain, what is clear is that it is crucial to apply the monofilaments in a consistent manner.

However, the optimal method of application remains uncertain. The procedures described to monitor sensation have varied and included mapping areas of altered peripheral nerve supply (Braun, Davidson & Doehr 1989; Gelberman et al. 1983) or scoring the peripheral nerves using a hand screen (Bell-Krotoski 1992, 2002; Szabo, R M, Gelberman & Dimick 1984). Monofilaments have been applied in ascending (Schulz, Bohannon & Morgan 1998) or descending order (Bell-Krotoski 1992, 2002) at specific sites. The decisions to determine thresholds have been based on whether a monofilament could be detected on one of up to three

applications (Bell-Krotoski 1992, 2002) on have varied by whether the monofilament was detected on every application or less frequently(Schulz, Bohannon & Morgan 1998).

The validity of monofilaments for testing touch perception is demonstrated by their ability to detect areas of abnormal sensation due to various diagnoses and document and monitor changes in peripheral nerve status (Bell-Krotoski 1995; Koris et al. 1990; Villarroel et al. 2007; Vinik et al. 1995). Monofilaments have been sensitive to recovery of light touch following surgery. Elevated thresholds for light touch affecting fingers innervated by the median nerve has been shown to improve or recover by six weeks after carpal tunnel release (Jimenez et al. 1993; Szabo, R M, Gelberman & Dimick 1984) and monofilaments have also been shown to be responsive to recovery following median nerve repair (Jerosch-Herold 2003).

Whilst monofilaments have demonstrated reliability and validity in monitoring peripheral nerve function, the scale for loss of light touch has been criticised. Monofilament values were selected from clinical experience of the associated loss in function. Consequently, the scale is ordinal, with increasingly wide intervals between forces (fig 2.4) and this has implications for the detection of reduced sensation and for methods of analysis (Patel & Bassini 1999).

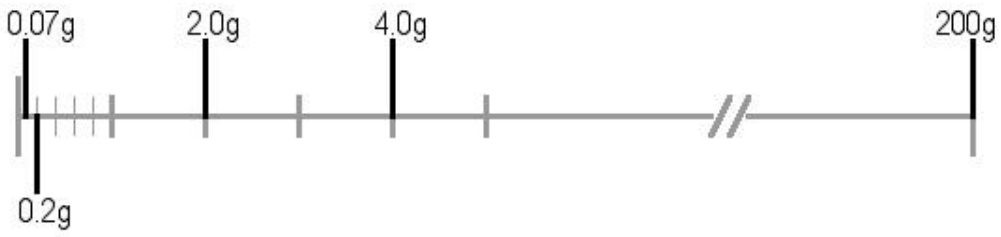

Figure 2.3 Consecutive WEST monofilaments apply forces with disparate intervals

2.7.3 INFLUENCES ON LIGHT TOUCH PERCEPTION

Recognising the force of the 0.07 gram WEST monofilament on up to three repeated applications at a site has indicated normal light touch perception with a sensitivity from 87% to 94% in the hand (Bowen, Griener & Jones 1990). However, later studies have questioned this result and determined various influences on an individual's threshold of light touch. The detection of light touch

can diminish with aging (Desrosiers et al. 1996), from skin calluses on the hands from manual work (Bell-Krotoski 1995) or can differ due to normal human variability in the sensory innervations of the hand (Massy-Westropp, N. 2002). The decline in light touch perception associated with aging may also be greater in men. Men older than 55 years of age could detect the two lighter monofilaments less consistently than women (Schulz, Bohannon & Morgan 1998).

2.7.4 RELATIONSHIPS WITH PHYSICAL FUNCTIONING

A small number of studies have found inconsistent relationships between tactile feedback and dextrous use of the hands. Light touch perception has correlated with recognising and handling objects with dexterity (Melchior, Vatine & Weiss 2007) and has been reduced in disabling peripheral neuropathy (Bell-Krotoski 1992). However, it has been poorly related to function in carpal tunnel syndrome (Levine et al. 1993) and with learning to read using Braille following visual loss (Nakada & Dellon 1989).

2.7.5 PROTOCOL

The peripheral nerve supply of the hand was tested using a hand screen designed for using with the five monofilaments in the WEST set. Seven sites were tested for each hand (fig 2.5). The three sites for the median nerve were the tip of the thumb, and the tip and base of the index finger. The three sites for the ulnar nerve were the tip and base of the little finger and the ulnar side of the palm. The site for the radial nerve was the dorsal aspect of the thumb web space (Bell-Krotoski 2002).

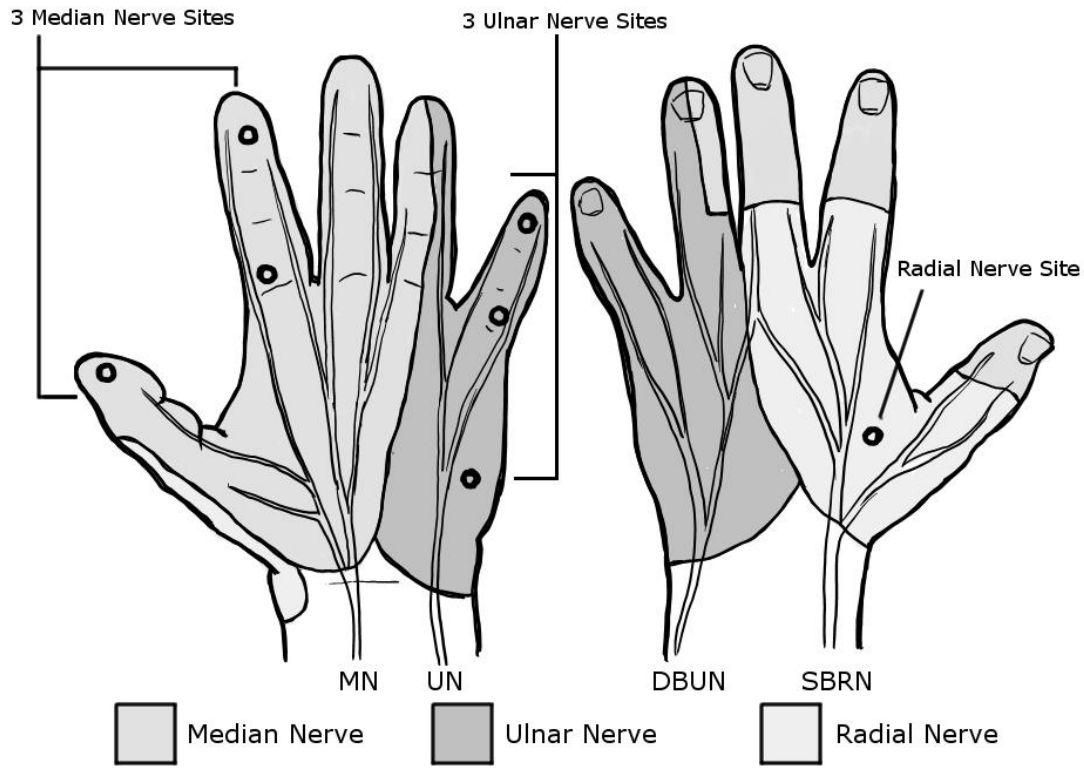

Figure 2.4 Sensory test sites in relation to the peripheral nerve supply
MN = median nerve UN = ulnar nerve DBRN = Dorsal branch of the ulnar nerve
SBRN = Superficial branch of the ulnar nerve

The dominant hand was tested before the non-dominant hand. First, the patient was familiarised with the procedure at a site on the forearm. Then, with the participant's eyes closed, the filaments were applied to the skin of the hand with up to three repeated applications at a site, until the touch was recognised by the participant. Each of the seven sites on the hand screen was tested. Testing started with the lightest monofilaments and proceeding to successively heavier filaments until the touch was felt.

Each site was given a score out of five depending on which of the filaments was the threshold of touch. The lightest filament scored as five and successively heavier filaments scored a point less. Totalling the scores from the seven sites each hand could get a maximum score of 35 that denoted that the perception of light touch was normal across the hand.

2.8 Nine-hole peg test of dexterity

2.8.1 DESCRIPTION

Finger dexterity was assessed by observing and timing the performance of the 9-hole peg test. The 9-hole peg test is a simple test of dexterity and one of the simpler tests available. It was designed to assess the fine coordination of the fingers by measuring the time in seconds to complete the accurate placement and removing of small pegs from a pegboard (fig 2.6).

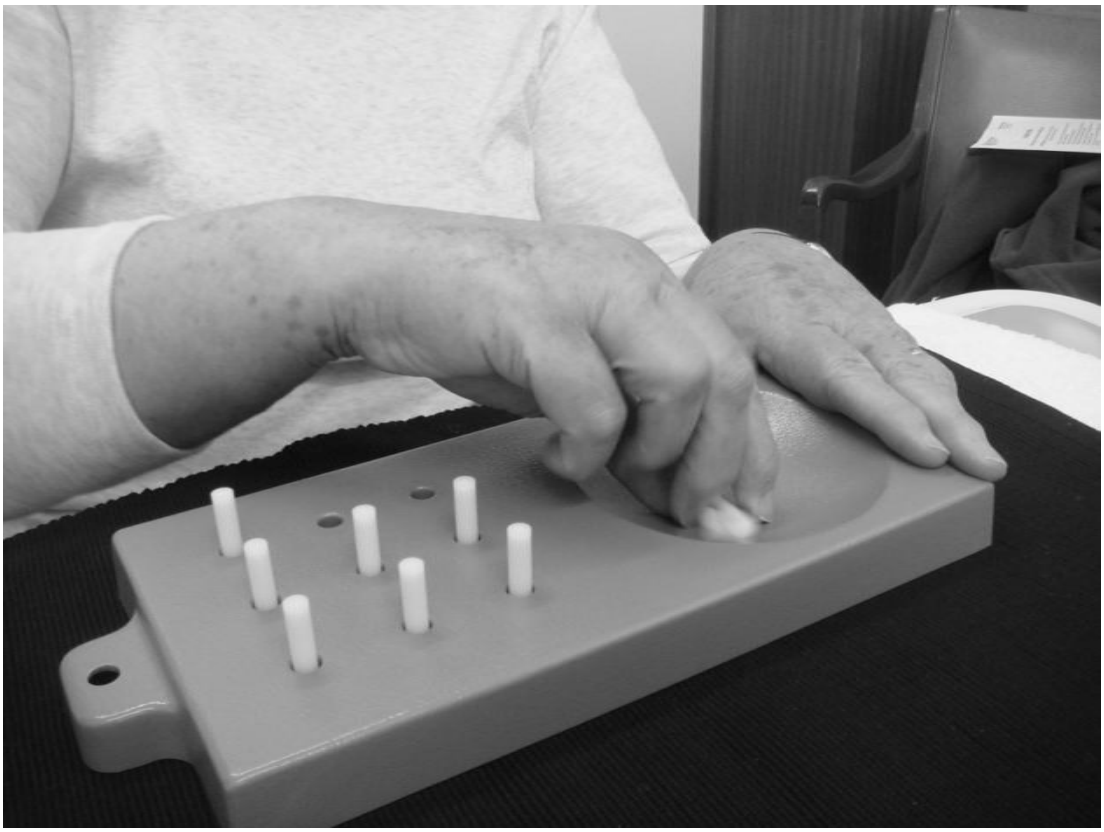

Figure 2.5 The 9-hole peg test measures the time to complete the accurate placement and removal of small pegs from a pegboard

2.8.2 RELIABILITY, VALIDITY AND SENSITIVITY TO CHANGE

The 9-hole peg test has been reliable in the general population (Mathiowetz, Weber, et al. 1985; Oxford Grice et al. 2003) and in people with Charcot-Marie-Tooth disease, although the slowest performers had more variable results (Svensson & Hager-Ross 2006). When the mean result of three trials was used, rather than one, results were more reliable (Oxford Grice et al. 2003).

Support for the concurrent validity of the nine-hole peg test as a test of dexterity is provided by correlations with the performance of other more complex dexterity tests (Backman et al. 1992). The evidence for the responsiveness of the nine-hole peg test is limited to a single study evaluating recovery following carpal tunnel release. Accelerated recovery of dexterity was described in response to a post-operative rehabilitation programme (Provinciali et al. 2000).

2.8.3 RELATIONSHIPS WITH PHYSICAL FUNCTIONING

The 9-hole peg test has been used to evaluate the everyday task of brushing the teeth. It was one of four dexterity tests that were related to the skilled manipulation of a toothbrush in order to effectively clean the teeth (Felder et al. 1994).

2.8.4 PROTOCOL

The 9-hole peg test that was used was manufactured by Rolyan (Huthwaite, Nottinghamshire). Each hand was tested separately and the procedures were standardised (Mathiowetz, Weber, et al. 1985):

- First, the examiner instructed the participant whilst briefly demonstrating the test.
- Next, a practice trial of dominant hand was allowed. The pegboard was placed on a table in front of the study participant with the container holding the pegs on the same side as the hand being tested.
- Then the timed test of dominant hand was completed. The test result was the time taken to pick up the pegs from the container one at a time, place them to fill the holes of the pegboard and then remove them back to the container one at a time. The examiner started the stopwatch after the instructions, “Are you ready? Go!” The examiner encouraged speed mid-test saying, “Out again...faster!” as the last peg filled the ninth hole of the pegboard. The stopwatch was stopped when the last of the pegs was removed back to the container. If the participant dropped a peg during the timed test, then the test was repeated.
- Then the pegboard was turned so the container was on the non-dominant side and the practice trial and timed test were repeated for the non-dominant hand.

2.9 Measuring obesity and history of diabetes

As part of the clinical examination, participants were asked if they had Type 1 or Type 2 diabetes, the number of years since they were diagnosis, their medications for diabetes and if complications were present. A self-reported history of laser eye surgery was used as a marker for retinopathy. A diagnosis of nephropathy or distal symmetrical neuropathy and HbA1c results were taken from case records or were provided by the participant's medical practitioner.

Each participant's weight and height were measured to calculate their body mass index (BMI). The BMI was calculated as weight (kg) divided by the square of the height (m^2). Individuals fitting into different ranges of BMI were classified as healthy, overweight or obese (healthy weight range ≥ 20 to < 25, overweight ≥ 25 to < 30, obese ≥ 30).

2.10 Subject selection and exclusion criteria

Participants were recruited from Modbury Hospital orthopaedic and diabetic outpatient clinics and from private orthopaedic or rheumatology practices. Diagnoses of diabetes and one of the four associated disorders was required for participation. These hand syndromes are diagnosed by characteristic symptoms, except for carpal tunnel syndrome, which is confirmed by nerve conduction studies. Diagnoses, other than the associated disorders, that could adversely affect hand function or a past history of significant trauma to the hands were exclusion criteria.

Inclusion criteria:

- Male or female
- Aged over 18 years
- Type 1 and Type 2 diabetes
- Associated hand disorder: Carpal Tunnel Syndrome, trigger finger, atypical Dupuytren's Disease or Limited Joint Mobility

Exclusion criteria:

- Rheumatoid arthritis
- Central nervous system disorders e.g. CVA or Parkinson's disease
- Significant visual impairment

- Recent hand fracture (< 6 months)

2.11 Sample size calculation

Table 2.3 displays the parameters used to calculate sample size for the DASH scores. A mean change of 10 points was estimated to be clinically important. The variability was estimated at 20 points (Greenslade et al. 2004) at each time point and the standard deviation of the difference was calculated from the standard deviations assuming zero covariance. Zero covariance would not be true, given that the same patients would be observed over time; consequently the sample size was conservatively overestimated. The minimum sample size required at 80% and 90% power was 126 and 169 respectively.

Table 2.3 Calculated sample sizes to detect a change of 10 DASH points with 80% and 90% power

SD = standard deviation

Parameters	DASH	DASH
T-test (1 or 2 sided)	2	2
Significance of test (α)	0.05	0.05
Power (%)	80%	90%
Estimated SD 1	20	20
Estimated SD 2	20	20
Estimated SD difference	28.28	28.28
Estimated mean 1	41	41
Estimated mean 2	51	51
Minimum difference	10	10
Calculated sample size	126	169

2.12 Ethics approval

Approval for the study was granted by the Modbury Hospital Research and Ethics Committee on 31 August, 2005. All participants gave informed consent prior to inclusion in the study.

2.13 Summary

- The rationale for selecting the instruments to assess hand function is discussed.
- The performance of the instruments is reported and reviewed.
- Protocols for hand assessments are described.
- The assessment included:
    - Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire
    - Short-Form 36-item Health Survey, version 2 (SF-36v2)
    - Dynamometer measurement of grip strength
    - WEST monofilaments measurement of light touch perception
    - 9-hole peg test that examines finger dexterity
    - measures of obesity, diabetes duration and control
- Grip strength has been related to physical functioning and disability.
- Light touch perception has been inconsistently related to tasks requiring dexterity.
- the 9-hole peg test has been shown to be reliable in the general population but requires further evidence for assessing a change in hand function
- Gender, aging and other individual factors can affect different aspects of hand function to varying degrees.
- The sample size to detect a change in hand disability was estimated.

CHAPTER 3. FACTORS ASSOCIATED WITH POORER HAND FUNCTION

3.1 Introduction

Adults with diabetes are at increased risk of functional limitations and physical disability that can reduce their quality of life. Research in this area has mainly focused on restricted mobility, but difficulties with activities of daily living, such as "cooking meals", that requires a level of hand function have also been documented (Gregg et al. 2002). Factors associated with physical disability include the personal characteristics of older age and female gender; the diabetic complications of cardiovascular disease, peripheral vascular disease, neuropathy and visual impairment; the co-morbidities of stroke and depression; and obesity (Bruce, Davis & Davis 2005; Dolan et al. 2002; Gregg et al. 2000; Gregg et al. 2002; Maggi et al. 2004; Resnick et al. 2002; Ryerson et al. 2003; Volpato et al. 2002; Von Korff et al. 2005; Wray & Blaum 2001). A loss of muscular strength, including grip strength, has also been associated with the development of physical disability in diabetes (Park et al. 2006; Sayer et al. 2005).

The contribution of the hand syndromes associated with diabetes to limitations of activities of daily living and disability is less clearly understood. Two reports have been published in this area. One showed a relationship between disability of the hand and grip strength, rather than the soft tissue syndromes (Savas et al. 2007). The other showed that reduced sensation of the hand, attributed to neuropathy in longstanding diabetes, was associated with difficulties with activities of daily living (Cederlund et al. 2009).

Although the treatments offered for these hand disorders are similar in diabetes as in the general population, there are differences in outcomes (Ozkul et al. 2002; Stahl, Kanter & Karnielli 1997). Recognising features of a presentation that may have an effect on outcomes is an important part of clinical assessment. The purpose of this study was to determine patterns of disability in the hand syndromes related to diabetes. In addition, factors associated with reduced hand function in adults with diabetes were evaluated.

3.2 Materials and methods

3.2.1 PARTICIPANTS

Sixty adults with type 1 or 2 diabetes and at least one of the associated hand disorders were recruited by clinicians working in diabetic and orthopaedic outpatient clinics at a public hospital, as well as private rheumatology and orthopaedic practices located in Adelaide, South Australia. They were recruited from February 2006 to March 2008 and the follow-up assessments ended in March 2010.

Participants were required to give written informed consent. The study was approved by the Modbury Hospital Research Ethics committee.

3.2.2 CLINICAL CHARACTERISTICS

An observational cohort study evaluating hand function was conducted. Demographic information and information on hand symptoms were collected by interview. Case records were reviewed to obtain HbA1c levels and a history of neuropathy and nephropathy. Retinopathy was accepted if the participant reported laser eye surgery. Body mass index was calculated from measured height and weight (BMI = kg/m^2).

Hand syndromes were diagnosed from characteristic clinical features (Kapoor & Sibbitt 1989; Moore 2000; Noble, Heathcote & Cohen 1984) or prior surgery for the disorder and, for carpal tunnel syndrome, symptoms were confirmed by nerve conduction studies (Rempel et al. 1998).

3.2.3 SELF-REPORT INSTRUMENTS

Two questionnaires were used to measure hand disability and health status. The Disabilities of the Arm, Shoulder and Hand (DASH) is a validated questionnaire that measures upper limb symptoms and functional status (Beaton, Katz, et al. 2001; Hudak et al. 1996; SooHoo et al. 2002). It includes thirty questions with the option of five responses for each question. A score is calculated from zero to a maximum of 100 where higher scores indicating greater disability. Version 2 of the Medical Outcomes Study Short Form-36 (SF-36v2) is a generic health measure that yields eight scales as well as physical and mental health summary measures

(Ware, Kosinski & Dewey 2000). The scales are norm-based around the same average (50) and same standard deviation (10 points).

3.2.4 TESTS OF HAND FUNCTION

Assessments were performed by one investigator (CL Redmond). Hand grip strength, light touch perception and the ability to use the fingers with dexterity were measured. Hand grip strength was measured with a calibrated EVAL electrodynamometer (Greenleaf Medical Systems, Palo Alto, CA, USA) using a standardised protocol (Mathiowetz, Kashman, et al. 1985). Light touch perception was measured with the WEST hand set of monofilaments (Connecticut Bioinstruments, Riverdale, NY, USA). The hand screening protocol measured the lightest of the five monofilaments that was felt when applied across seven sites covering the peripheral nerve supply of the hand (Bell-Krotoski 1992). Of the seven sites, three areas were supplied by median and ulnar nerves respectively and one area was supplied by the radial nerve (maximum score = 35). Finger dexterity was measured by the time to complete the Rolyan nine hole peg test (Homecraft Rolyan, Notts, UK) using a standardised protocol (Mathiowetz, Weber, et al. 1985). Scores from the dominant hand were used in the analyses.

3.2.5 DATA ANALYSIS

All scores were tested for normality and the decision to use parametric or non-parametric statistics was based on the distribution of data. Normative data, available for some variables, were used to compare with the sample data. As the results of the DASH questionnaire were skewed, the differences between groups were evaluated with Mann-Whitney U tests and the strength of association was evaluated with Spearman correlation coefficients. Variables hypothesised to be potential mediators of disability were included in step-wise multiple regression models to obtain an optimum set of predictor variables. Significance level was set at $p < 0.05$ for all tests. Statistical analyses were performed with Intercooled Stata 10.0 for Windows (2008, StataCorp, College Station, TX, USA).

3.3 Results

3.3.1 CLINICAL CHARACTERISTICS

Of the 60 participants (34 females, 57%), complete data were available for 59 (98%), as the questionnaires were not completed by one participant. The clinical characteristics of the study population are shown in Table 1. Four diagnoses related to the hands in diabetes were represented in both sexes. Twenty seven participants (45%) had carpal tunnel syndrome, twenty four (40%) had trigger finger, sixteen (27%) had Dupuytren's disease and fifteen (25%) had limited joint mobility. However, the diagnostic categories were not independent, as it was common for participants to present with more than one hand syndrome, as current symptoms or in their past history (n = 28, 47%).

Table 3.1 Clinical features associated with diabetes and the diagnosed hand disorder in males, females and the total sample

Values are the number (percentage) unless otherwise indicated. SD=standard deviation BMI=body mass index IQR=interquartile range HbA_{1c}= glycosylated haemoglobin (%)

	Males (n=26)	Females (n=34)	Total (n=60)
Age, mean (SD),years	59.4 (10.7)	62.1 (10.2)	60.9 (10.5)
BMI, median (IQR), kg/m^2	29.2 (28.4, 31.5)	29.3 (26.3, 39.1)	29.2 (26.7, 32.9)
Duration diabetes, median (IQR),years	11.5 (7,22)	16.5 (8,28)	14.5 (7,28)
HbA_{1c}, mean (SD)	7.4 (1.3)	7.7 (1.7)	7.6 (1.5)
Type 1 diabetes	6 (23%)	9 (26%)	15 (25%)
Retinopathy	5 (19%)	9 (26%)	14 (23%)
Nephropathy	5 (19%)	9 (26%)	14 (23%)
Neuropathy	1 (4%)	4 (12%)	5 (8%)
Insulin	13 (50%)	20 (59%)	33 (55%)
Carpal tunnel syndrome	9 (35%)	18 (53%)	27 (45%)
Trigger finger	12 (46%)	12 (35%)	24 (40%)
Dupuytren's disease	5 (19%)	11 (32%)	16 (27%)
Limited joint mobility	10 (38%)	5 (15%)	15 (25%)

3.3.2 SELF-REPORT INSTRUMENTS

Levels of hand disability for each hand disorder, as measured by the DASH, are presented in Figure 3.1. There were no significant differences in disability related to the hand disorder but the influence of gender was apparent. In the study population, women reported more disability, with significantly greater DASH scores than men (mean (CI), 30.3 (23.2, 37.5) vs. 18.0 (12.1, 23.9), $p = 0.01$).

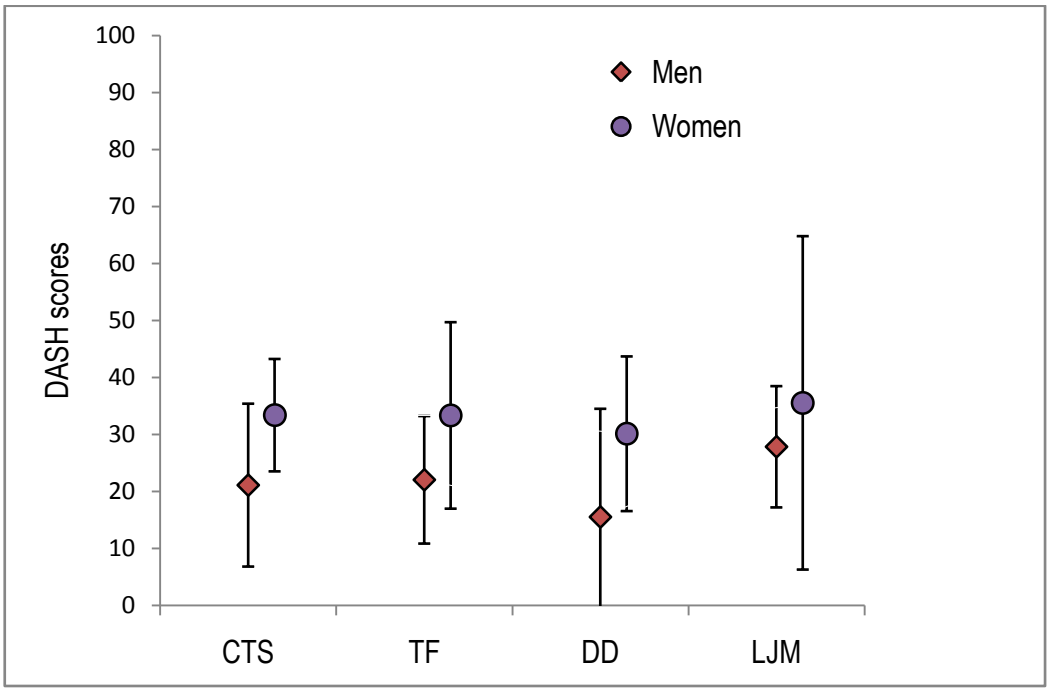

Figure 3.1 DASH scores of males and females for each hand disorder. Means with 95% Confidence Intervals; CTS: carpal tunnel syndrome; TF: trigger finger; DD: atypical Dupuytren's disease; LJM: limited joint mobility

Our sample of adults with diabetes was characterised by poor physical health. The physical component summary score of the SF-36 was less than expected for age and gender matched norms (Ware, Kosinski & Dewey 2000) ($p < 0.05$). The mental component summary score was similar to population normative data. The scales of the SF-36 were not significantly influenced by gender, although there was a borderline difference ($p = 0.07$) in physical functioning (Table 2). We postulated that this may be a Type 2 error, and that a larger sample size would have demonstrated that females have poorer physical function.

Table 3.2 Mean (SD) and p values of Short Form 36 scales reported at initial assessment for males and females

SF-36 scale	Males (n=26)	Females (n=33)	P value
Physical functioning	43.4 (9.4)	38.3 (11.6)	0.07
Role physical	43.4 (9.9)	42.4 (11.2)	0.71
Bodily pain	43.0 (8.9)	42.1 (8.6)	0.70
General health	42.7 (10.2)	39.7 (11.7)	0.31
Vitality	48.2(11.6)	47.5 (9.4)	0.80
Social functioning	47.2 (11.2)	47.9 (10.8)	0.80
Role emotional	44.8 (14.2)	44.1 (14.1)	0.85
Mental health	48.9 (11.3)	48.5 (11.7)	0.88

3.3.3 TESTS OF HAND FUNCTION

Our sample was characterised by reduced grip strength. Mean grip strength was significantly less than expected for age and gender matched norms (Mathiowetz, Kashman, et al. 1985) ($p < 0.05$). Gender influenced grip strength. Males had a mean (SD) grip strength of 39.1 kg (1.9) and women had a mean of 23.2 kg (1.2), which was significantly less ($p < 0.0001$).

Our sample was also characterised by reduced sensation affecting the hands of both men and women. Generally, this was a symmetrical finding with light touch perception of the dominant hand being similar to the non-dominant hand ($r = 0.83$, $p < 0.0001$). In addition to those with carpal tunnel syndrome, sensation was reduced in participants with a past history of carpal tunnel release, peripheral neuropathy affecting the feet, or the syndrome of limited joint mobility. When testing thresholds in impaired sensation, the light touch of the 0.07 g WEST monofilament that denotes normal cannot be felt and the threshold changes to a stiffer filament applying a heavier force. In the median nerve distribution, at the tip of the index finger of the dominant hand, 87% of participants had diminished light touch, below the normal threshold of the 0.07 g monofilament. In addition, 62% of participants had diminished protective sensation, with a threshold below the heavier touch of the 0.02 g monofilament. Similarly, in the ulnar nerve distribution at the tip of the little finger of the dominant hand 72% of participants

had a threshold below the normal 0.07 gm, 38% of participants had diminished protective sensation with a threshold below 0.02 g and one participant (2%) had a threshold below the 2.0 g filament.

The median (IQR) time to complete the 9-hole peg test of dexterity was 20.3 seconds (18.3, 23.7) and was not influenced by gender. This measure of dextrous performance had a stronger correlation with sensation scores (r = -0.71, $p < 0.0001$) than with grip strength (r = -0.33, $p = 0.009$).

3.3.4 FACTORS ASSOCIATED WITH HAND DISABILITY

Significant relationships between hand disability and the eight scales of the SF-36 were demonstrated. These ranged from a strong relationship (-0.71, $p < 0.001$) for the physical functioning scale to a moderate relationship (-0.39, $p = 0.002$) for the mental health scale. Hand disability was also related to the hand function tests. Hand disability correlated moderately with grip strength (-0.54, $p < 0.001$), the performance of the nine hole peg test of dexterity (0.55, $p < 0.001$) and weakly with sensation (-0.29, $p = 0.02$). There were inter-correlations between variables. Grip strength, sensation and dexterity were also related to physical functioning (0.51 to 0.31, $p < 0.05$), and body mass index had weak relationships to both physical functioning (-0.34, $p = 0.009$) and hand disability (0.26, $p = 0.05$).

Variables that had a linear relationship with hand disability of $p < 0.20$ were included in two multiple linear regression models (Tables 3 and 4). The first model examined health status and included the scales of the SF-36, BMI, gender and duration of diabetes. The second model examined hand function and included grip strength, sensation and dexterity, BMI, gender and duration of diabetes.

For the health status model that explained 66% of the variance, the predicted hand disability was 100.1 – (0.8 x Physical Functioning) – (7.8 x gender) – (0.5 x Bodily Pain) – (0.4 x Vitality) where males = 1 and females = 0. For the hand function model that explained 36% of the variance, the predicted hand disability was -2.7 – (0.6 x grip strength) + (1.1 x dexterity) + (0.7 x BMI).

Table 3.3 Regression analysis of health status variables that predicted hand disability

	Coefficient of β	Standard error of β	P value	95% Confidence Interval	
Physical functioning	-0.75	0.18	<0.001	-1.11	-0.40
Gender	-7.78	3.0	0.012	-13.77	-1.77
Bodily pain	-0.52	0.22	0.022	-0.97	-0.07
Vitality	0.40	0.19	0.038	-0.77	-0.02
Constant	100.1	7.9	<0.001	84.24	115.94
Adjusted R^2= 0.66					

Table 3.4 Regression analysis of hand function variables that predicted hand disability

	Coefficient of β	Standard error of β	P value	95% Confidence Interval	
Grip strength	-0.64	0.19	0.001	-1.01	-0.27
Dexterity	1.12	0.40	0.007	0.33	1.93
BMI	0.72	0.32	0.030	0.07	1.38
Adjusted R^2= 0.38					

3.4 Discussion

In this study, the relationships between self-reported instruments and assessments of hand function were investigated. The SF-36 and the tests of hand function showed significant correlations with the DASH that ranged from -0.71 for the physical functioning scale to -0.29 for the light touch perception scores of the WEST hand monofilaments. The International Classification of Functioning, Disability and Health (ICF) have proposed a classification of functioning, at levels of impairment, activity limitation and participation restriction that is influenced by personal and contextual factors (World Health Organisation 2001). The relationships demonstrated between impairments of hand function and limitations of activity influenced by gender and aspects of physical or mental health support this theoretical model. Disability was not related to age or to the control of blood sugar levels but did reflect the complex interplay of a number of different factors.

3.4.1 GENDER

We identified that women had greater limitations of daily activities from these hand syndromes. While it has previously been established that women with diabetes have greater physical limitations, the contribution of these musculoskeletal conditions to limitations of hand function in women is a new finding. Despite the heterogeneity of clinical presentations, higher levels of disability reported in women could be reflecting the dominance of carpal tunnel syndrome affecting hand function. However, it could also be reflecting that a of a loss of upper body strength has a greater impact in women; because women have significantly less grip strength, a decline in strength will result in an increased proportion of maximal capacity being required for daily activities.

3.4.2 OBESITY

Obesity, a known risk factor for carpal tunnel syndrome (Becker et al. 2002), independently predicted hand disability. It is also a known risk factor for mobility difficulties in women (Wray & Blaum 2001). This suggests that hand disability is related to an interaction of obesity and carpal tunnel syndrome, but may also be part of an overall decline in physical functioning. In women, difficulties using the hands for activities of daily living may have co-existed with restricted mobility, as the DASH was strongly associated with the physical functioning scale of the SF-36. This is similar to the report of generalised physical disability found in elderly patients with Type 2 diabetes (Bruce, Davis & Davis 2005).

3.4.3 STRENGTH

We demonstrated that reduced grip strength was related to disability of the hands. This is consistent with previous findings (Savas et al. 2007). Pain, finger joint stiffness, flexor muscle or tendon shortening, carpal tunnel syndrome, lower levels of physical activity and the negative influence of diabetes and obesity on muscle quality could all contribute to poor muscle function and hand weakness. Grip strength was also related to physical functioning, which is consistent with prior reports that grip strength can be used as a measure of whole body strength and physical disability (Davis, JW et al. 1998; Giampaoli et al. 1999).

This study provides clues that exercise may be a suitable strategy to address reduced grip strength. However, because it is likely that hand disability results from multiple factors, the influences of pain, restricted movement, psychological factors and the functional requirements of the individual should be considered before effective strengthening can occur. Randomised controlled trials of the effects of exercise in preventing limitations of hand function and disability in diabetes are needed.

3.4.4 SENSATION

We demonstrated that loss of light touch affected the performance of tasks requiring dexterity and was related to disability of the hands. Most participants had sensory impairment affecting the fingertips, in areas supplied by the median and also the ulnar nerves. Similar patterns of sensory changes in the hands have been previously demonstrated in diabetes (Cederlund et al. 2009; Chochinov, Ullyot & Moorhouse 1972) and in carpal tunnel syndrome (Jimenez et al. 1993). Therefore, it is interesting to speculate that generalised peripheral neuropathy or thickening of the skin, due to increased glycosylation of connective tissue proteins, may have contributed to the loss of light touch from median nerve entrapment. An area for future research is to investigate the relationships between light touch perception, the glycosylation of tissues and findings from nerve conduction studies.

3.4.5 LIMITATIONS OF THIS STUDY

The results of this study should be viewed in the light of some limitations. The sample may not be representative of all adults with the hand syndromes related to diabetes as participants were recruited from patients referred to orthopaedic surgeons, rheumatologists or hospital diabetes clinics, and those seeking treatment may have more disabling symptoms. In contrast to the two other publications in this area, carpal tunnel syndrome or a history of carpal tunnel release were common and are likely to have influenced levels of hand impairment and disability in this study. The diagnoses relating to the hands were often mixed and while this made interpretation by diagnostic category difficult, presenting with

alteration in a variety of soft tissue structures of the hand can occur in longstanding diabetes.

A number of confounders were not analysed. Co-morbidities are known to influence physical disability and may have negatively influenced the physical functioning of the women in the study. There were insufficient participants with Type 1 diabetes enrolled in the study to present separate analyses. The characterisation of hand disability in Type 1 diabetes remains an area requiring further investigation.

Although the instruments were selected as being valid and reliable, all instruments have strengths and limitations. A limitation of measuring grip strength is that no distinction is made between the contribution of pain, finger stiffness or muscle weakness to the values recorded. The determination of normal light touch perception using the WEST hand monofilaments is an area of controversy (MacDermid, J C, Kramer & Roth 1994) particularly in older adults (Desrosiers et al. 1996). The nine hole peg test is a simple test of dexterity, that may not detect subtle limitations of performance.

3.4.6 SIGNIFICANCE OF THIS WORK

Despite these limitations our results support supplementing self-reported hand disability with impairment, performance and health status measures. The measures were related but highlighted different aspects of hand functioning and suggested that multiple factors contributed to hand disability, including physiological and psychological factors.

Assessment of the hands in diabetes, and monitoring of carpal tunnel syndrome, trigger finger, Dupuytren's disease and limited joint mobility is relevant, as these syndromes can cause difficulties with daily tasks requiring strength or dexterity. Using tests that are suitable for use in the clinic, we also demonstrated that reduced sensation, influenced by carpal tunnel syndrome, contributed to disability. This study emphasised the interrelationships between the hands, obesity and overall physical functioning in women. Maintaining dexterity and upper body strength; managing pain; and encouraging a healthy weight are important strategies to minimise disability in the hand syndromes associated with diabetes.

3.5 Summary

- This study determined patterns of disability in diabetic hand conditions and identified factors that contributed to functional limitations.
- The most frequent presentation was carpal tunnel syndrome (45%) but it was common to present with clinical features associated with more than one hand syndrome (47%).
- Overall, women had greater difficulties than men (mean (CI) 30.3 (23.2, 37.5) vs. 18.0 (12.1, 23.9), $p = 0.01$).
- Grip strength, dexterity and obesity independently predicted hand disability.
- Aspects of physical and mental health also independently predicted hand disability.

CHAPTER 4. DETECTING DETERIORATING HAND FUNCTION

4.1 Introduction

This purpose of this study was to evaluate deteriorating hand function in diabetes-associated hand disorders during a two-year period. We hypothesised that change may be accelerated in particular aspects of hand function, secondary to these hand disorders. In addition, comparisons with published norms analysed with initial data were extended to include data from subsequent assessments.

The aims of this chapter were to:

- further characterise the hand function and health-related quality of life of adults with hand disorders associated with diabetes
- identify factors associated with deteriorating hand function during a two-year period

In order to achieve these aims, the objectives were to:

- compare hand function measures with population norms at each assessment
    - compare grip strength with population norms
    - compare tactile sensation with population norms
    - compare the performance of dexterity with population norms
    - compare symptoms and function, as measured by the DASH, with population norms at each assessment
- compare health related quality of life profiles with population norms, using SF-36v2 norm-based scoring, at each assessment
- identify aspects of hand function that changed over subsequent annual clinical assessments and determine what factors were associated with this change

4.2 Methods

The analysis presents results from interpreting the data collected during the two-year period of the study. Our study observed hand functioning during three assessments periods. Initial assessments were followed by two annual reviews. The median follow up for the second assessment was 13 months (range 12 to 19 months) and for the third assessment was 30 months (range 25 to 40 months).

Data from each of the assessed and self-reported measures are reported for the three assessments.

Each analysis is displayed with a graph or table that is accompanied by text explaining the results.

4.3 Statistical analysis

Statistical analyses were performed with Intercooled Stata 10.0 for Windows (2008, StataCorp, College Station, TX, USA). The distribution of data analysed with parametric tests was displayed with means and 95% confidence intervals. *T*-tests were used with these data to test for significant differences between the study sample and the normative data, as well as between the first and subsequent assessments. All tests were two tailed and $p < 0.05$ was considered statistically significant.

The sensory data was analysed by non-parametric tests and displayed with box and whisker plots. The Wilcoxon matched-pairs signed-ranks test was used to test for significant differences between the study sample and normative data, as well as between the first and subsequent assessments.

In the sub-analyses of the effect of gender and the dominant hand on grip strength and dexterity, group means were compared using *t*-tests. For the sub-analyses on tactile sensory scores, equality tests on matched and unmatched data were used. The medians were compared between each hand using the Wilcoxon matched-pairs signed-ranks test. The medians were compared between men and women using the Wilcoxon rank-sum test, which is also known as the Mann-Whitney two-sample statistic (StataCorp 2005).

4.4 Results

Hand function was compared at each assessment to population norms.

4.4.1 RATES OF FOLLOW-UP

We enrolled 60 participants. During two years of follow-up, eight participants withdrew, three were unable to be contacted and one died. At the first and third assessments, one participant did not return questionnaires. At the first annual review (median, 13 months; range, 12-19 months), the rate of follow-up was 88%. This dropped to 80% at the second review (median, 27 months; range, 25-40 months), which reduced the power to analyse small changes in hand function.

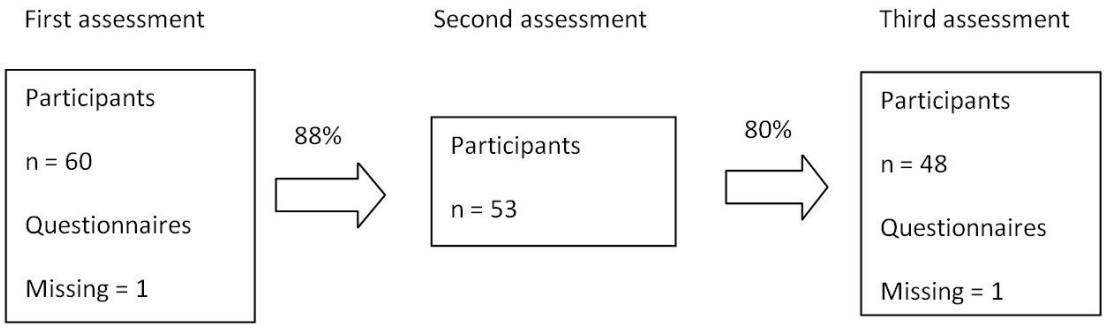

Figure 4.1 Loss to follow-up at each assessment

4.4.2 DISABILITY OF THE ARM, SHOULDER AND HAND (DASH) QUESTIONNAIRE

This analysis assessed the disability levels associated with the hand disorders in this study sample by comparing DASH scores with unadjusted (Hunsaker et al. 2002) and age-adjusted norms (Jester, Harth & Germann 2005). The latter study sampled employed adults and categorised their results into the age groups of 18 to 29 years, 30 to 49 years and 50 to 65 years. For the analysis, the upper age category was modified to include all those aged over 50 years.

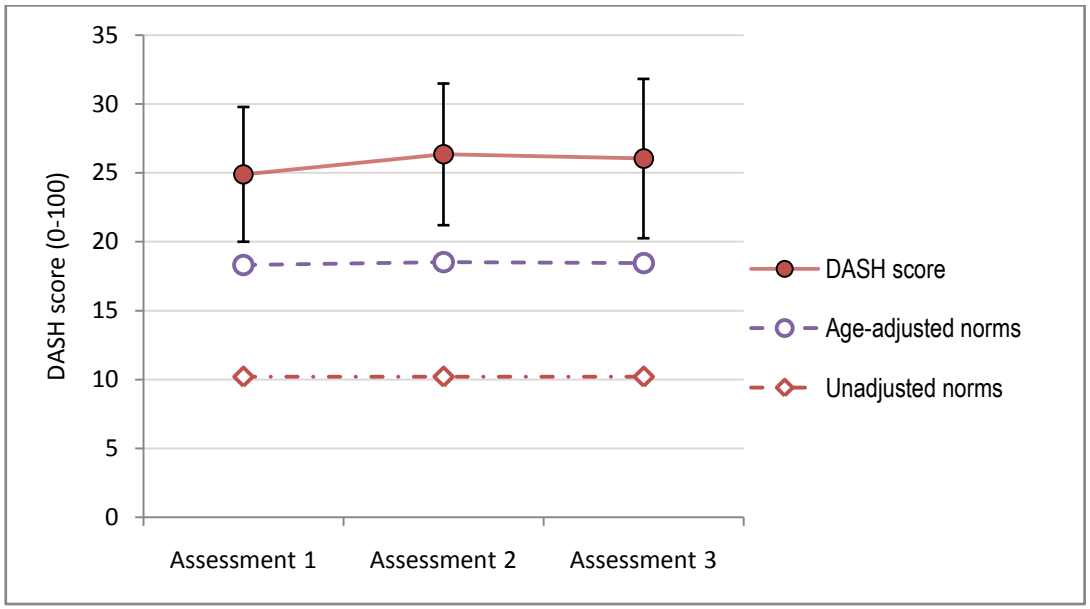

Figure 4.2 DASH scores compared with unadjusted and age-adjusted norms at each assessment

Mean with 95% confidence intervals

The disability levels associated with these hand disorders were significantly greater compared to adjusted population norms (Assessment 1, $p = 0.01$; Assessment 2, $p = 0.004$; Assessment 3, $p = 0.01$) (fig. 4.1).

Disability levels did not significantly change during the two-year period.

4.4.3 GRIP STRENGTH

This analysis assessed grip weakness associated with the study population by comparing the grip strength force of each hand with age and gender adjusted norms (Mathiowetz, Kashman, et al. 1985).

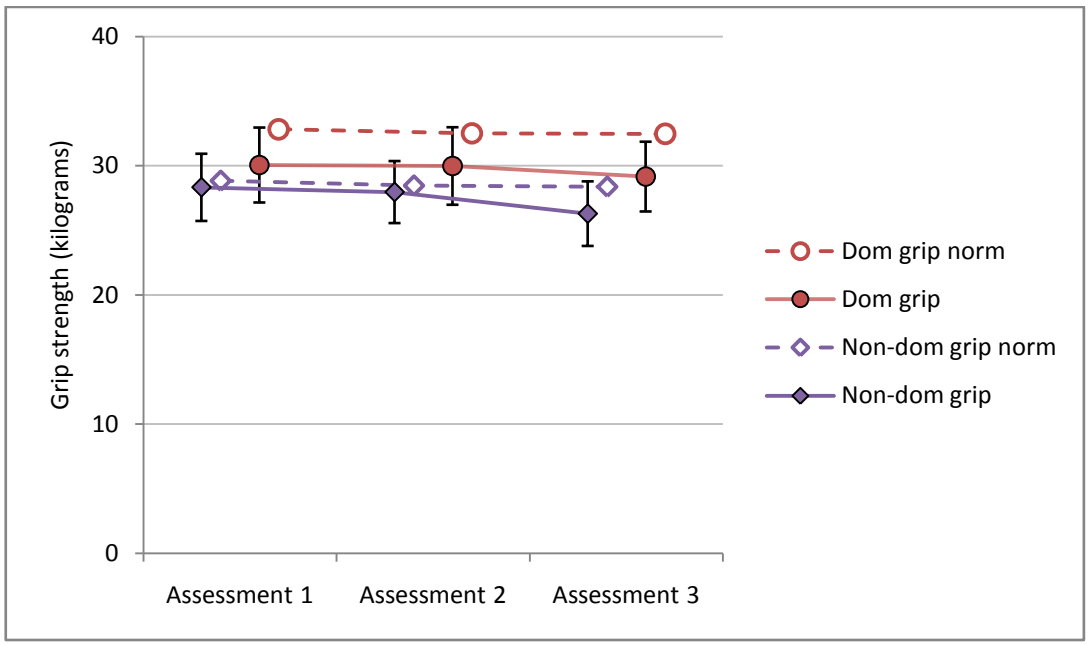

Figure 4.3 Grip strength for each hand compared with norms at each assessment
Mean with 95% confidence intervals

The dominant hand had significantly weaker mean grip strength compared to matched normative means at the first and third assessments (fig. 4.2). The difference at the second assessment from the normative mean was not significance (Assessment 1, $p = 0.04$; Assessment 2, $p = 0.06$; Assessment 3, $p=0.007$)

The non-dominant hand had mean grip strengths that were not significantly different to matched normative means.

Grip strength did not significantly change during the two-year period.

4.4.4 DEXTERITY

This analysis assessed poorer dexterity associated with the study population by comparing times to complete the 9-hole peg test with age and gender adjusted normative data for the right and left hands (Mathiowetz, Weber, et al. 1985).

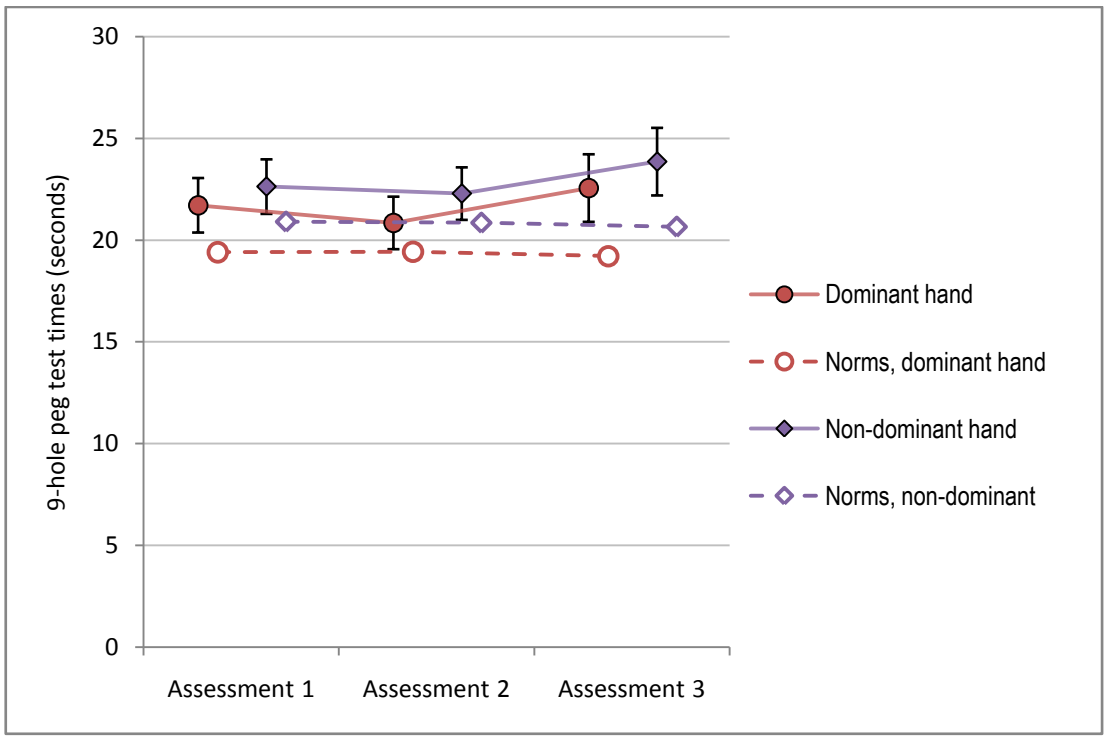

Figure 4.4 Nine-hole peg test times for each hand compared with normative times
Mean with 95% confidence intervals

The dominant hand took significantly longer to complete the 9-hole peg test of finger dexterity than matched normative values (Assessment 1, $p = 0.002$; Assessment 2, $p = 0.03$; Assessment 3, $p < 0.001$) (fig. 4.3).

The non-dominant hand took significantly longer to complete the 9-hole peg test of finger dexterity than matched normative values (Assessment 1, $p = 0.02$; Assessment 2, $p = 0.04$; Assessment 3, $p = 0.002$)

Dexterity did not significantly change during the two-year period.

4.4.5 HAND SENSATION

This analysis assessed reduced light touch perception associated with the study population by comparing hand sensation screen scores with sensory norms. The WEST 0.07g monofilament, designated the value of 5, has been considered the normal threshold for touch perception. Normal sensory perception would score a subtotal of 15 points for the median nerve, 15 for the ulnar nerve and 5 for the radial nerve, for a total of 35 points across the hand sensation screen (Bell-Krotoski 1995).

However, more recent evidence suggests that normal monofilament values should be adjusted for age and gender (Desrosiers et al, 1996, Shultz et al, 1998). More recent normative values have been determined for three categories: men and women aged 55 years or younger, 0.035g; women over 55 years, 0.15g; and men over 55 years, 0.385g (Schulz, Bohannon & Morgan 1998).

These norms are estimates of thresholds for touch perception, generated using the rapid threshold procedure. These estimates were generated from the results that 80% of men and women 55 years of age or younger consistently reported feeling the 0.07g filament (i.e., value of 5), 80% of women older than 55 years consistently reported feeling the 0.2g filament (i.e., value of 4) and 80% of men older than 55 years less consistently reported feeling the 0.2g filament (i.e., value of 4).

This analysis compared the study sample with three categories of adjusted normative scores. Men and women less than 55 years of age were matched to normative scores of 35, women 55 years of age and older was matched to a normative score of 28 and men 55 years and older were more conservatively matched to a normative score of 25.

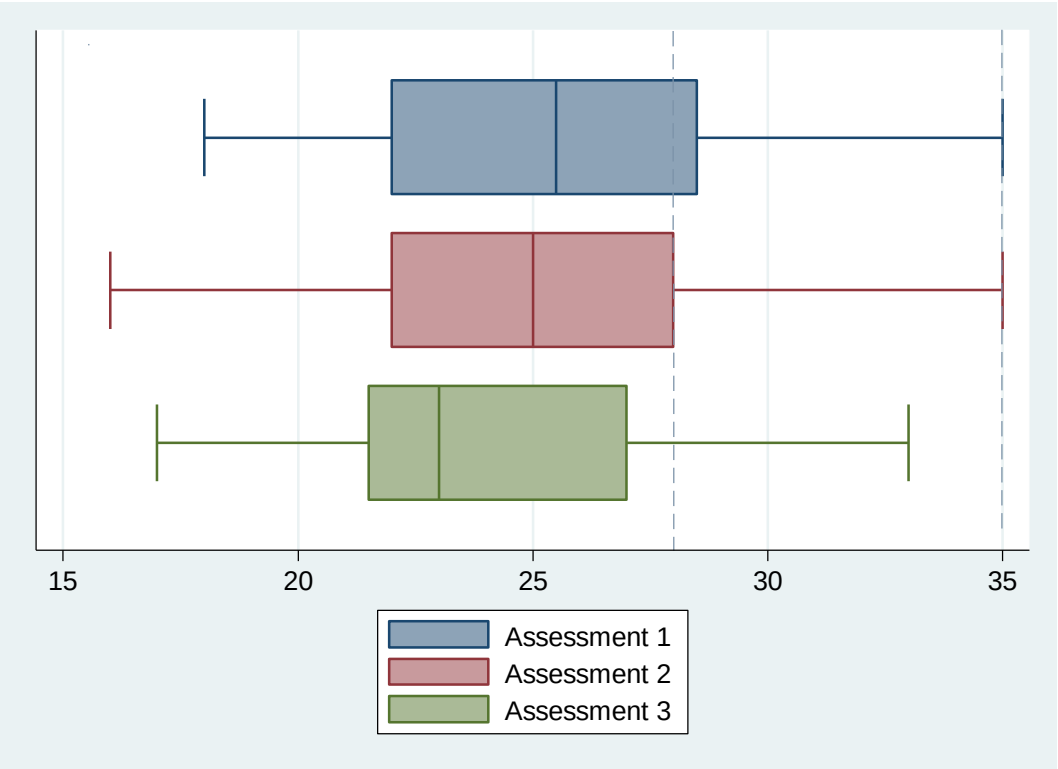

Figure 4.5 Tactile sensation scores from the dominant hand at each assessment
Median (vertical line); 25th and 75th percentiles (box); range (whiskers)

WEST monofilament scores were significantly diminished in the dominant hand compared to age-adjusted normative scores at each assessment ($p < 0.001$) (fig. 4.4).

WEST monofilament scores were significantly diminished in the non-dominant hand compared to age-adjusted normative scores at each assessment ($p < 0.001$).

Tactile sensation deteriorated in the dominant hand during the two-year period ($p = 0.03$).

4.4.6 HEALTH-RELATED QUALITY OF LIFE

This study presents the norm-based results from the SF-36v2 scores of study participants. Norm-based scoring applies a linear T-score transformation (mean = 50, SD=10), which makes it possible to meaningfully compare scores for the eight-scale profile and the physical and mental summary measures across samples. General U.S. adult population statistics were used in this standardization of the SF-36v2 scores.

T-tests were used to test for significant differences between the health-related quality of life of the study sample, assessed by the standardised SF-36v2 scores of study participants, with population means for all scales and summary scores.

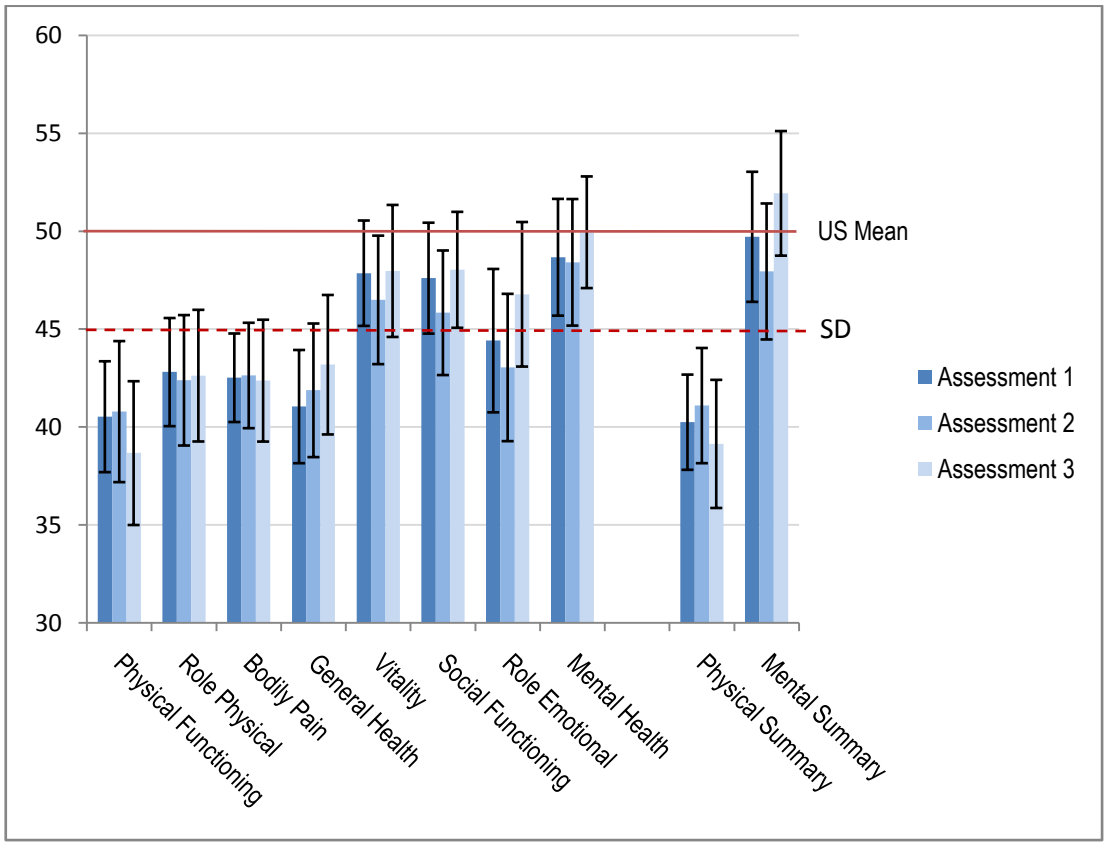

Figure 4.6 SF-36v2 scales and summary scores at each assessment
Mean with 95% confidence intervals

The impact of diabetes at each assessment was largest in scales assessing physical health concepts (fig. 4.5).

The greatest decrease compared to U.S. general population norms was seen in the Physical Functioning score, which had upper limits of the 95% confidence intervals outside the population standard deviation.

This pattern was clearly reflected in the summary measures, with the Physical Component Summary (PCS) below the population average at each assessment, while the Mental Component Summary (MCS) remained close to average.

Compared to the general population, the study participants reported:

- having greater limitations of physical activities
- accomplishing less as a result of physical problems
- having pain interfere with daily activities
- having poorer health.

Health-related quality of life did not significantly change during the two-year period.

4.5 The dominant hand and gender

4.5.1 GRIP STRENGTH

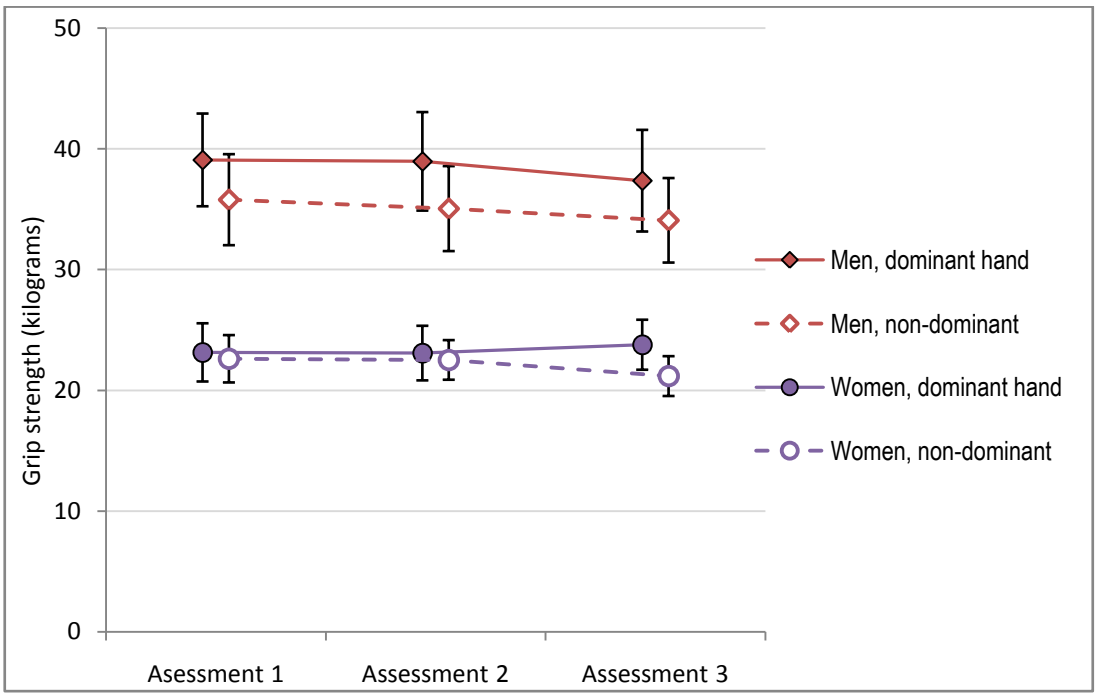

Figure 4.7 Grip strength for each hand of men and women
Mean with 95% confidence intervals

Grip strength was strongly influenced by gender ($p < 0.001$ at each assessment) (fig 4.6). On average, the men were approximately 40% stronger than the women (Assessment 1, mean, 41%; 95% CI, 30% to 52%).

The dominant hand was stronger than the non-dominant hand (Assessment 1, $p = 0.02$; Assessment 2, $p = 0.001$; Assessment 3, $p < 0.001$). Differences in strength between the hands were more substantial in men.

4.5.2 DEXTERITY

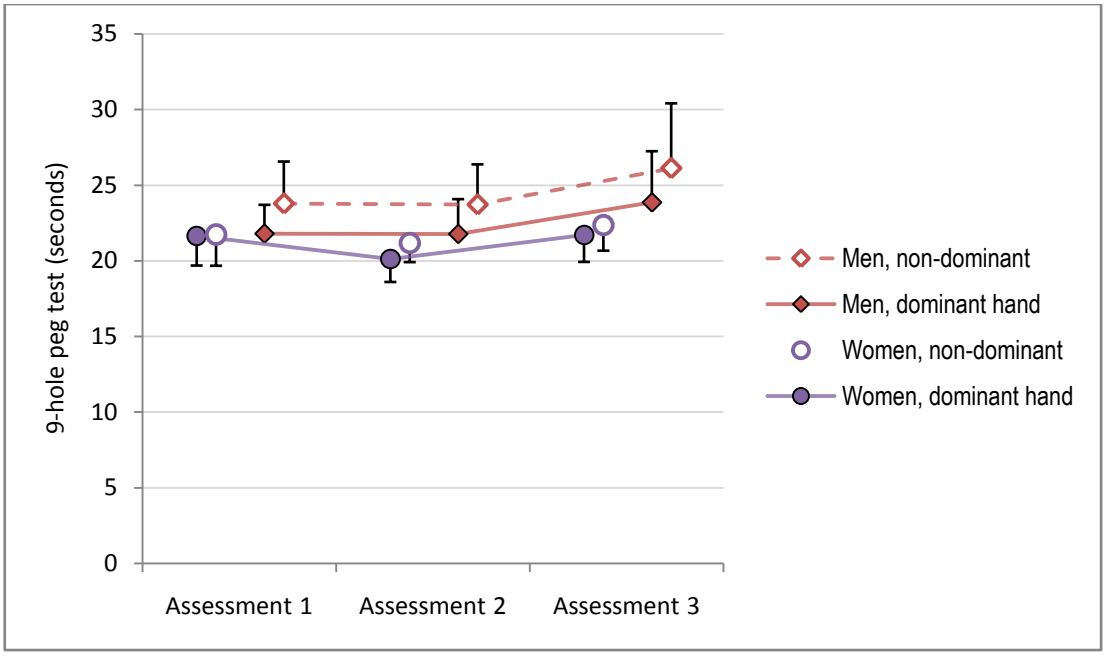

Figure 4.8 Nine-hole peg test times for each hand of men and women
Mean with 95% confidence intervals

The dominant hand and gender had more subtle effects on dexterity (fig. 4.7).

The dominant hand was faster at the second assessment ($p < 0.01$) but did not reach statistical significance at the third assessment ($p = 0.06$).

Differences between men and women in the performance of the 9-hole peg test did not reach statistical significance (Assessment 1, $p = 0.16$; Assessments two and three, $p = 0.06$).

4.5.3 SENSATION

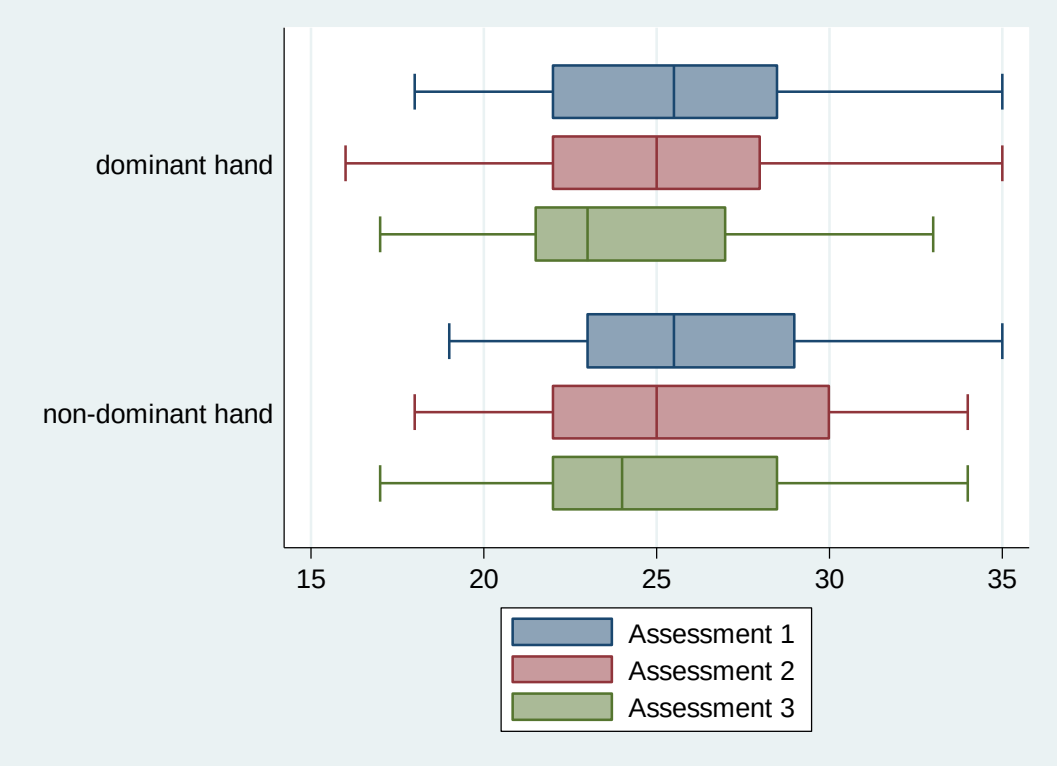

Figure 4.9 Tactile sensation scores calculated for both hands
Median (vertical line); 25th and 75th percentiles (box); range (whiskers)

Light touch perception was reduced bilaterally but there were subtle differences between the hands (fig. 4.8). WEST monofilament scores of the dominant hand were less compared to the non-dominant hand (Assessment 1, $p = 0.03$; Assessment 2, $p = 0.02$; Assessment 3, $p = 0.05$).

The dominant hand had an accelerated loss of light touch perception. WEST monofilament scores significantly deteriorated in the dominant hand ($p = 0.03$) during a two-year period, but did not significantly change in the non-dominant hand.

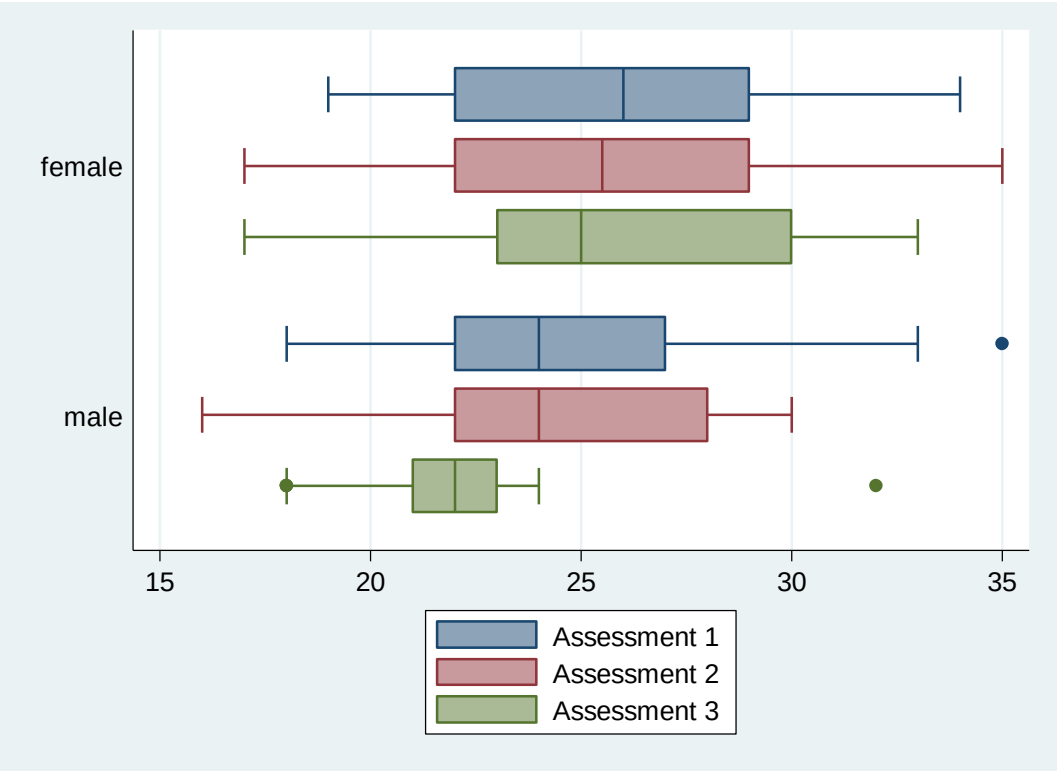

Figure 4.10 Sensory scores from examining the dominant hand, in men and women

Median (vertical line); 25th and 75th percentiles (box); range (whiskers); outlying values (filled circle)

Tactile sensation was reduced in both men and women. Differences in light touch perception between the sexes were found inconsistently.

WEST monofilament scores of the dominant hand were less in men at the third assessment (p = 0.003) (fig. 4.9).

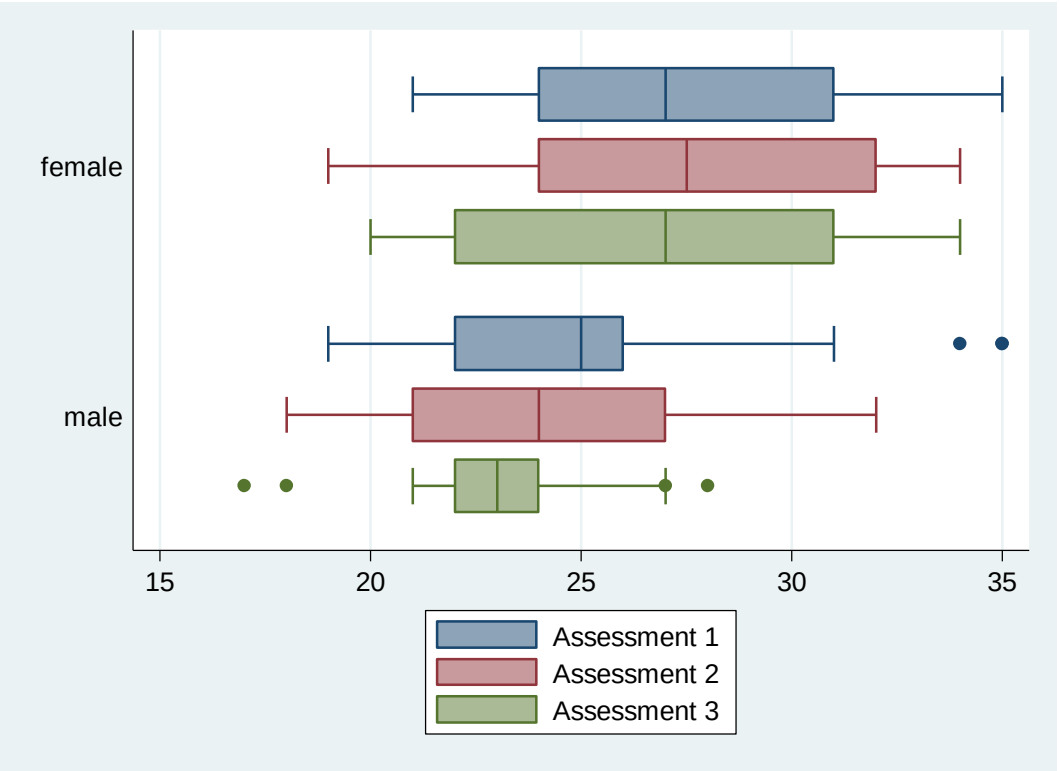

Figure 4.11 Sensory scores from examining the non-dominant hand, in men and women

Median (vertical line); 25th and 75th percentiles (box); range (whiskers); outlying values (filled circle)

WEST monofilament scores of the non-dominant hand were less in men at the first and third assessment, while the difference at the second assessment did not reach statistical significance (Assessment 1, $p = 0.02$; Assessment 2, $p = 0.06$; Assessment 3, $p = 0.02$) (fig. 4.10).

4.6 Sensory change analysis: trigger finger

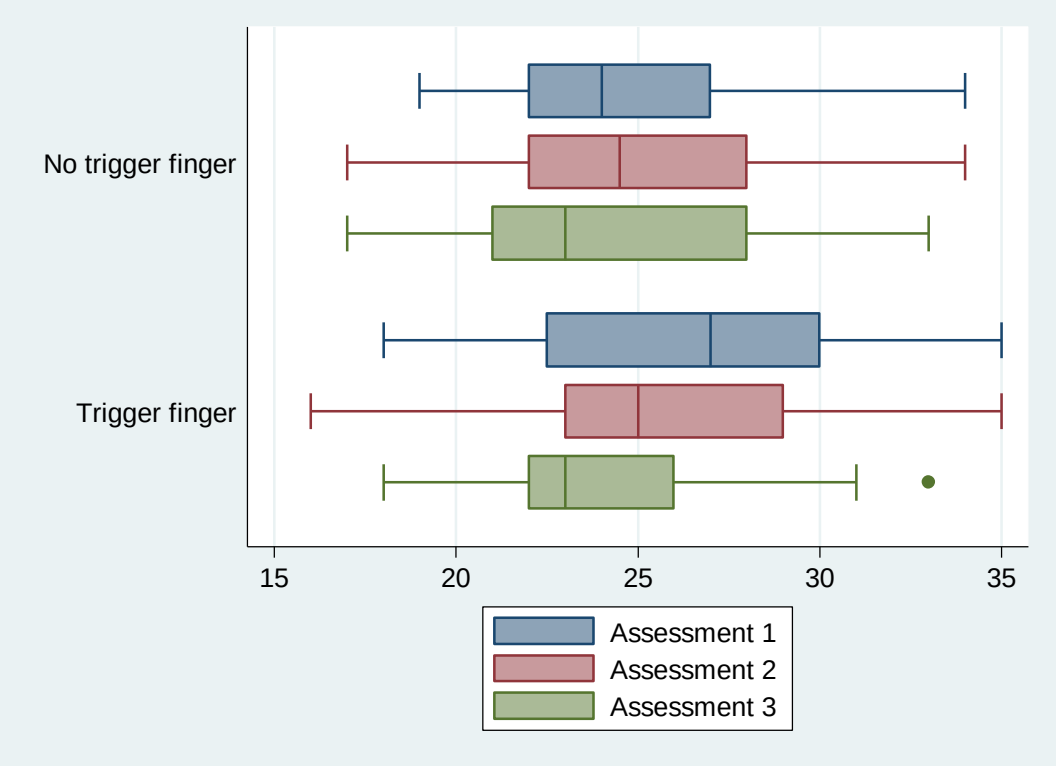

Figure 4.12 Sensory scores from examining the dominant hand, by trigger finger
Median (vertical line); 25th and 75th percentiles (box); range (whiskers); outlying value (filled circle)

WEST monofilament scores of the dominant hand significantly deteriorated between the first and third assessment in those with trigger finger (p = 0.05) (fig. 4.11).

WEST monofilament scores of the dominant hand did not significantly change during the assessment period for the other hand diagnoses.

4.7 Sensory change analysis: Hand surgery in the first year

During the course of the study, 12 participants (20%) had hand surgery.

Ten participants (17%) had hand surgery in the first year. Five patients had a carpal tunnel release, of which one had trigger finger releases performed as additional procedures. Four further patients had trigger finger releases and an additional patient had a Dupuytren's contracture released.

In the second year after enrolment, two of these patients had further surgery. One patient had revision of the carpal tunnel release and the patient with Dupuytren's contracture had the other hand released. Two further patients (3%) had carpal tunnel releases.

This analysis compared the sensory scores between those who had either a carpal tunnel release or trigger finger release in the first year.

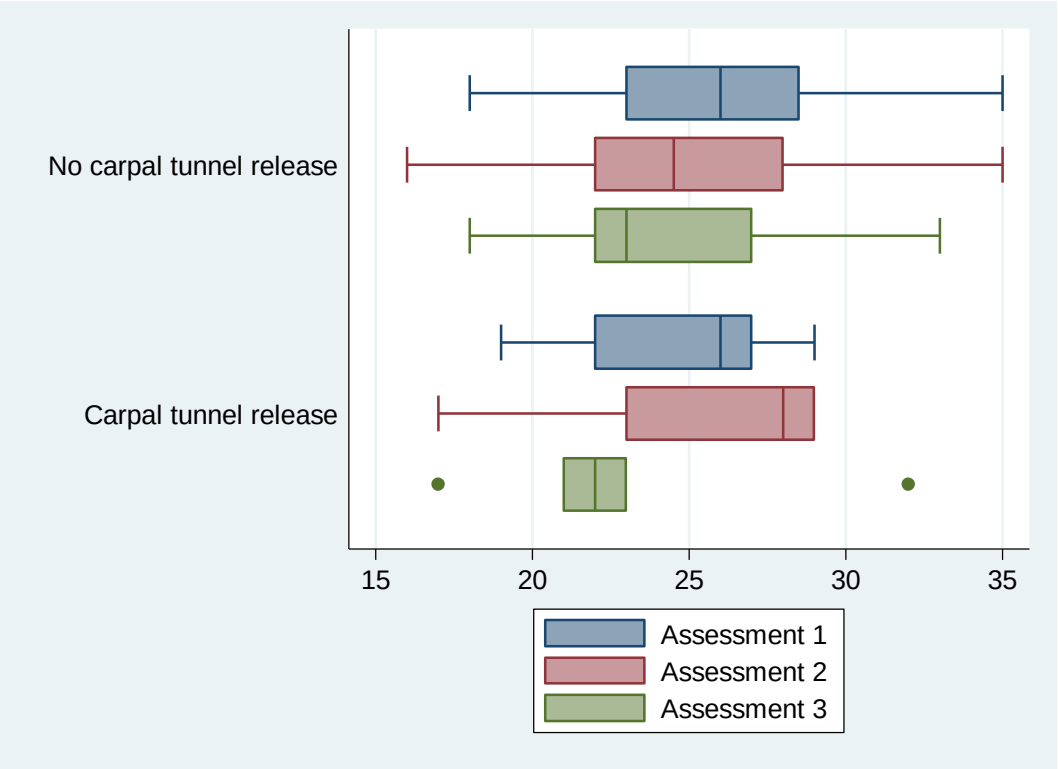

Figure 4.13 Sensory scores from examining the dominant hand, by carpal tunnel release during the first year

Median (vertical line); 25th and 75th percentiles (box); range (whiskers); outlying values (filled circle)

For those who had a carpal tunnel release during the first year, the WEST monofilament scores of the dominant hand did not significantly change between the first assessment and the second or third assessments (fig. 4.12).

This analysis lacked power because of the small numbers of patients involved.

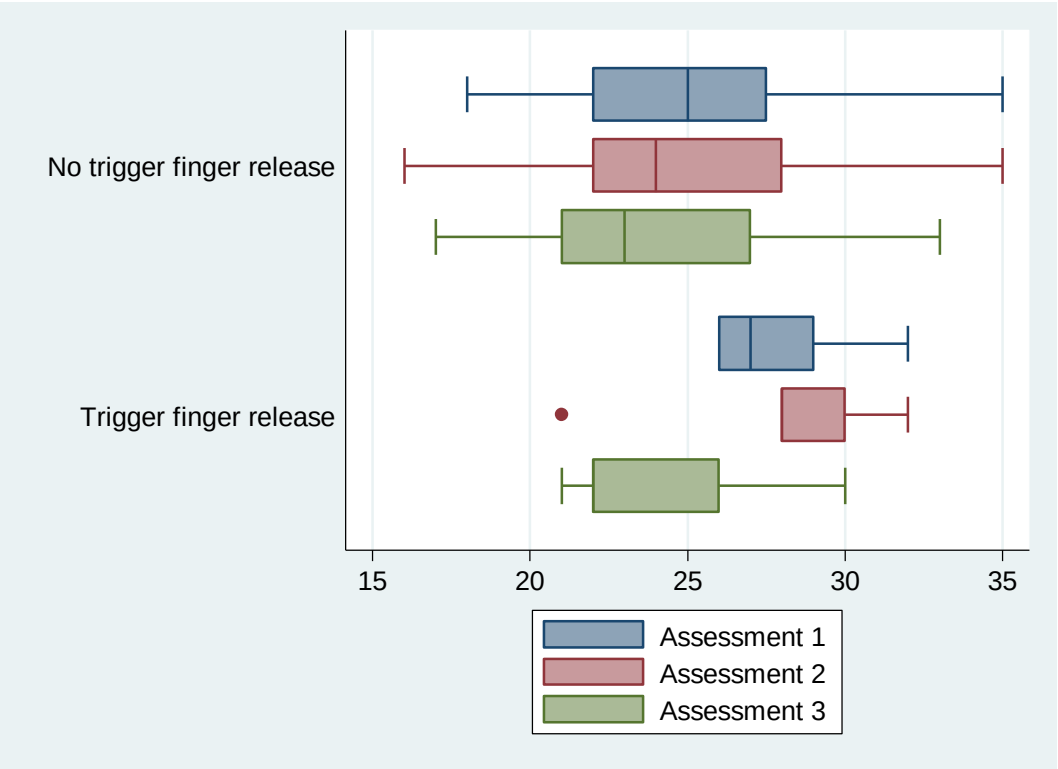

Figure 4.14 Sensory scores from examining the dominant hand, by trigger finger release during the first year

Median (vertical line); 25th and 75th percentiles (box); range (whiskers); outlying value (filled circle)

For those who had a trigger finger release during the first year, the WEST monofilament scores of the dominant hand did not significantly change between the first assessment and the second or third assessments (fig. 4.13).

This analysis lacked power because of the small numbers of patients involved.

4.8 Sensory change analysis: peripheral nerve supply

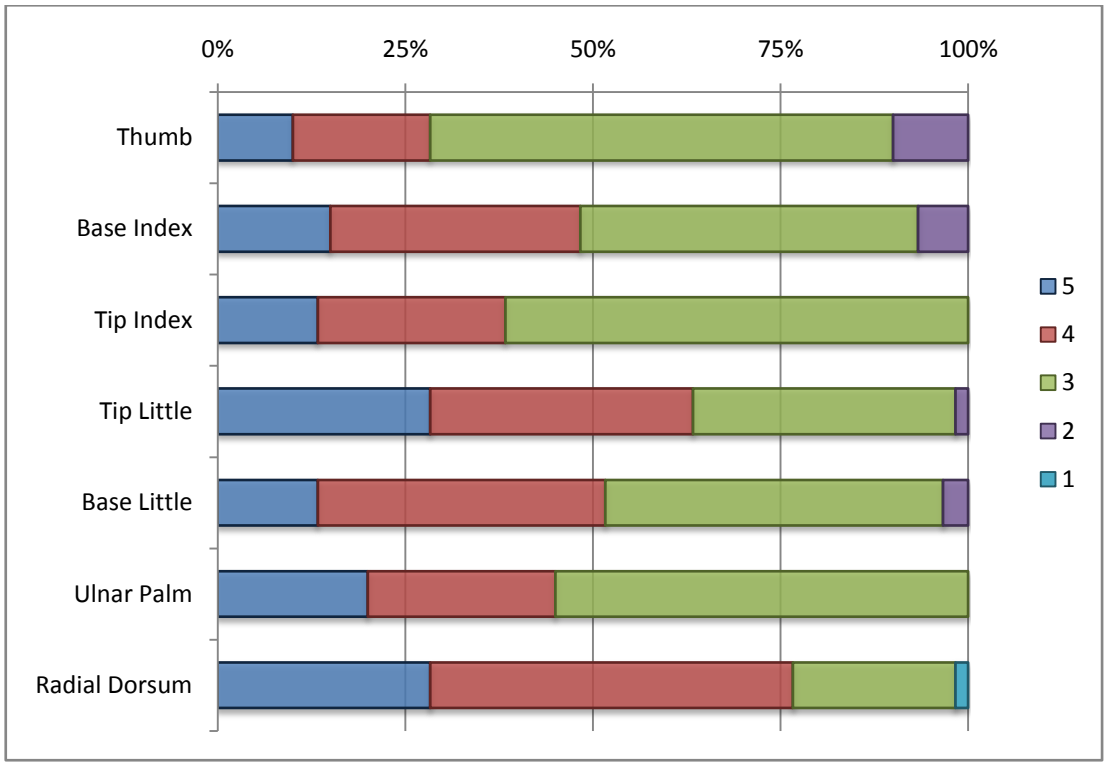

Figure 4.15 Proportions of monofilament thresholds felt at each dominant hand site

Monofilament values: 5, 0.07g; 4, 0.2g; 3, 2g; 2, 4g; 1, 200g.

At the start of the study, there were differences in light touch perception across the areas tested (fig. 4.14). The area tested on the thumb pad, supplied by the median nerve, was the least sensitive (median, 3; IQR, 4 to 3) and the area tested on the dorsum, supplied by the radial nerve, was the most sensitive (median, 4; IQR, 5 to 4).

Scores obtained using WEST monofilament testing were significantly less in the three areas supplied by the median nerve supply (median, 10; IQR, 9 to 12) compared to the three areas supplied by the ulnar nerve (median 11; IQR, 9 to 13) ($p < 0.001$).

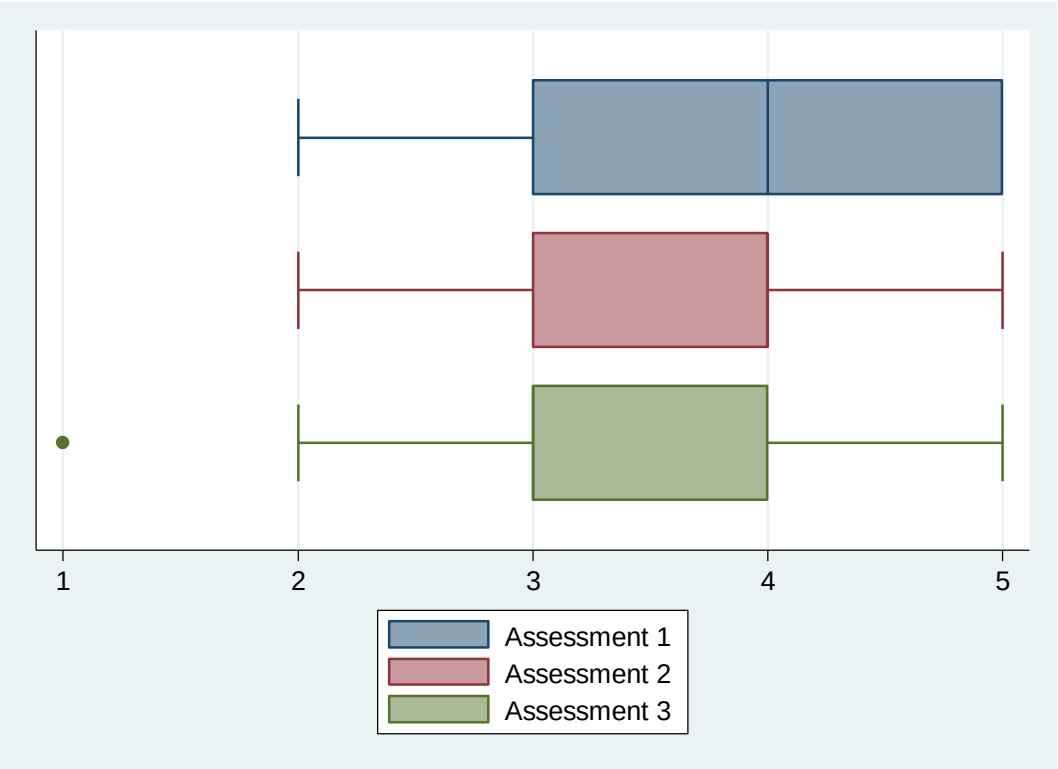

Figure 4.16 Monofilament values for the little finger tip
Median (vertical line); 25th and 75th percentiles (box); range (whiskers); outlying value (filled circle)

Between the first and third assessments, WEST monofilament scores significantly decreased at the little finger tip, supplied by the ulnar nerve (p <0.001) (fig. 4.15).

This was an early loss of light touch that reduced the differences between tactile sensation scores for the areas supplied by the median and ulnar nerves.

4.9 Body weight

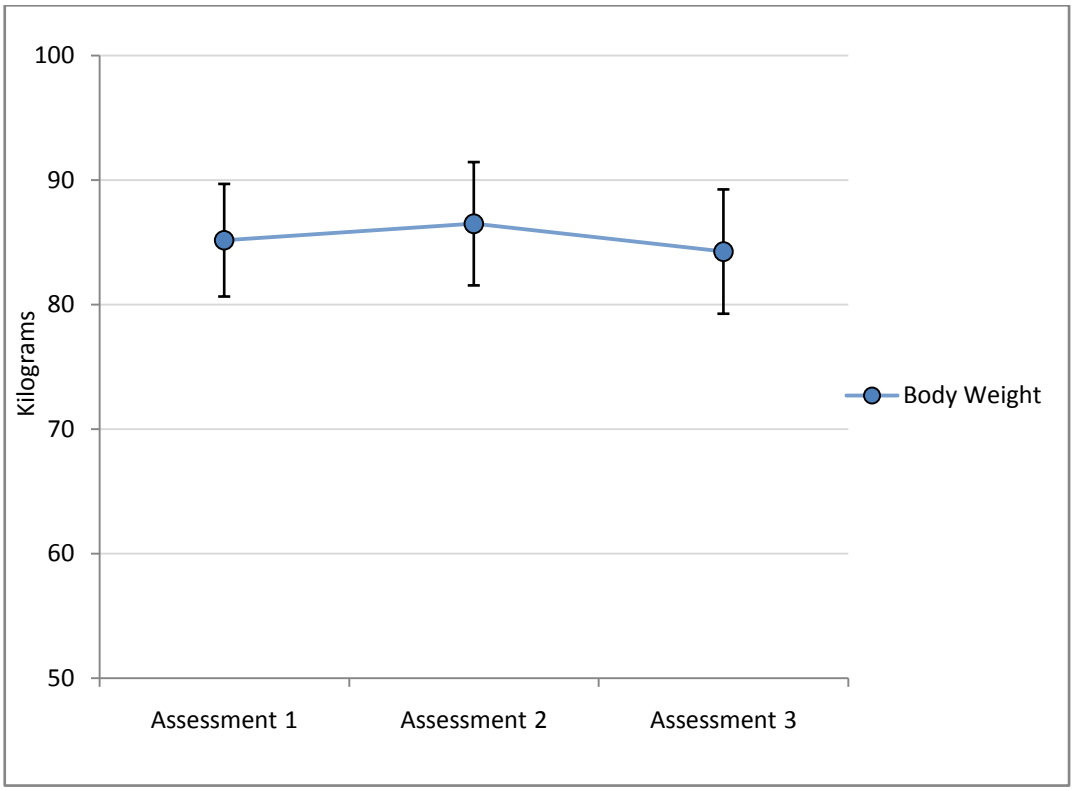

Figure 4.17 Body weight measurements of participants during a 2-year period
Mean with 95% confidence intervals

In this study, in which longstanding diabetes and obesity were common, body weight did not change significantly (fig 4.16).

Two patients had a sleeve gastrectomy performed in the second year, with successful weight loss of 14 and 36 kg during the two year period.

4.10 Assessment of characteristics of those lost to follow-up

This analysis compared the characteristics of those lost to follow-up with those who completed the study.

Table 4.1 Characteristics at study entry comparing participants who completed all assessments to participants who were lost to follow-up at assessment 2 or 3

Baseline Characteristic mean (SD)	Completed study (n=48)	Lost to follow-up (n=12)	p-value
Age (years)	60 (8)	64 (17)	0.25
Number, (%) of women	29 (60%)	5 (42%)	0.25
Diabetes duration (years)	20 (15)	13 (12)	0.18
HbA1c (%)	7.6 (1.2)	7.4 (2.7)	0.73
DASH (0-100 score)	26 (20)	19 (14)	0.26
SF-36 PCS (norm-based score)	40 (9)	40 (7)	0.92
SF-36 MCS (norm-based score)	51 (13)	46 (12)	0.24

When they entered the study, the characteristics of those lost to follow-up were similar to those who completed the study. Their age, proportion of each sex, years since being diagnosed with diabetes, control of diabetes, functional limitations and health-related quality of life did not significantly differ. However, there is potential bias introduced by those who did not complete the study.

4.11 Discussion

We determined that significant impairments of grip strength and tactile sensation may be associated with diabetes-associated hand disorders, when compared to normative values from the general population. Individuals may report high levels of pain and limitations of daily activities, as well as poor physical health. While limitations of mobility, and to a lesser extent, limitations of activities of daily living, have previously been associated with diabetes, our study demonstrated that hand disorders in diabetes can contribute to these difficulties.

4.11.1 ACTIVITIES OF DAILY LIVING

There are two recent studies that have investigated difficulties of daily living in diabetes-associated hand disorders. Our sample differed in a clinically important way as it included high proportions of patients with carpal tunnel syndrome (n = 27, 45%) and/or trigger finger (n =24, 40%). We believe that this difference resulted in the greater impact on activities of daily living found in our study. Cederlund et al, 2009 found difficulties with activities of daily living in elderly men with type 2 diabetes, attributed to diabetic neuropathy. These difficulties occurred in those with long-term diabetes, when tactile and vibration senses were impaired. Their study differed to ours, in that women were excluded, carpal tunnel syndrome and trigger finger were infrequently diagnosed and only a few patients had undergone surgery for these conditions.

Savas et al, 2007 found difficulties of daily living in hand disorders in type 2 diabetes, attributed to reduced grip strength. Our study supports their finding that reduced grip strength was common. However, their sample was substantially different to ours, in that carpal tunnel syndrome was excluded and trigger finger was an infrequent diagnosis. Of note, they also found that diabetic neuropathy commonly affected the hands but was not significantly related to difficulties with daily activities.

4.11.2 SENSATION

Our study found sensory abnormalities that were detected with WEST monofilaments. Tactile sensation was reduced in the thumb and index finger, as well as the little finger. Sensory abnormalities were generalised but were greatest

in the areas supplied by the median nerve. This finding suggests that median nerve entrapment develops on a background of subclinical peripheral neuropathy in diabetes. The index finger has previously been found to have reduced light touch in type 1 diabetes (Chochinov, Ullyot & Moorhouse 1972), as have the thumb, index and little fingers in type 2 diabetes (Cederlund et al. 2009). These findings have been attributed to diabetic neuropathy. However, abnormalities of light touch that affect the little finger, in addition to the index finger, have also been found in carpal tunnel syndrome in the general population. Consequently, it has also been proposed that the flexor retinaculum may tension Guyon's tunnel and cause subclinical compression of the ulnar nerve in carpal tunnel syndrome (Jimenez et al. 1993; MacDermid, J C, Kramer & Roth 1994). Therefore, diabetic neuropathy cannot be definitively distinguished from carpal tunnel syndrome by comparing the index to the little finger with monofilament testing. The task for future research is to compare monofilament testing with nerve conduction studies.

Monofilament thresholds have been related to levels of sensory impairment and functional limitations (Bell-Krotoski 2002). In our study, most of the group were at the levels designated as reduced tactile sensation or reduced protective sensation. Reduced tactile sensation was described as having minimal impact, so that it may not be noticed. Reduced protective sensation was described to result in diminished use of the hands, difficulty manipulating some objects and a tendency to drop objects. At entry into our study, there was a moderate relationship between poorer sensory scores and slower performance of dexterity that support these descriptions. However, poorer sensory scores were only weakly related to functional limitations, suggesting that there may have been differing abilities to adapt to or compensate for sensory deficits in this group. An alternative explanation is that dexterity tests may be more sensitive to difficulties manipulating small objects and, therefore, compliment results from administering the DASH questionnaire.

Different aspects of the group's measured hand function changed during two years. Tactile sensation deteriorated slightly in the dominant hand. In contrast, grip strength, functional limitations and health-related quality of life remained stable

over this time. WEST monofilaments were a sensitive measure of increasing sensory abnormalities during this period.

4.11.3 TRIGGER FINGER

The hand diagnosis group most affected by sensory change during the observation period was those with trigger finger. Explanations for an association between trigger finger and sensory deterioration are speculative. Patients presenting with coexisting carpal tunnel syndrome and trigger finger has previously been reported (Kumar & Chakrabarti 2009; Neal, McManners & Stirling 1987; Rottgers, Lewis & Wollstein 2009; von Schroeder & Botte 1996). This has generated conjecture on whether they share aetiological mechanisms or if synovial thickening from trigger finger, extending into the carpal tunnel, contributes to ischemia of the median nerve. In our study, this sensory change was subclinical in some individuals and associated with increasing symptoms, such as pins and needles, in others. Due to the lack of other evidence, and because the analysis is based on small numbers, further research into mechanisms that determine sensory change is required. However, we do recommend careful examination including screening for symptoms indicating carpal tunnel syndrome in patients with trigger finger; or the corollary, that it is important to screen for symptoms of trigger finger when patients with diabetes present with carpal tunnel syndrome.

4.11.4 THE DOMINANT HAND AND GENDER

Hand function was affected by hand dominance and gender, with more similarities than differences to prior descriptions in the general population. These patterns have been incorporated into better quality normative data that is stratified by age, gender and for tests administered to each hand separately, for the right and left hands.

The dominant hand has been described as about 5 to 10% stronger than the non-dominant hand (Bechtol 1954). This difference, described as 'the 10% rule', has been shown to be more relevant to right-handed individuals as left-handed individuals have hands that are more equivalent in strength (Petersen et al. 1989). It is difficult to interpret or compare the estimates from these studies, as their precision was not reported. In our study there was wide variation in percentage

differences in strength between the two hands. The dominant hand was 6% stronger than the non-dominant with a 95% confidence interval from 1% to 11%. Individuals presented with differing degrees of hand dominance that support the view that there are "many shades of hand preference" (Fess 1997). When comparing the hands, potential differences between them should be borne in mind.

Our results were consistent with studies indicating that women have greater tactile sensitivity. This has been attributed to differences in nerve function and skin condition with aging. Men have been described as developing more skin calluses, particularly if they have worked in manual occupations. Some individuals in our study had developed finger tip calluses from frequently applying finger prick tests to the pad of the finger. However, other skin changes were visible. Skin thickening associated with long-standing type 1 diabetes, was more apparent in men and may have been partly responsible for reducing tactile sensation.

An unexpected finding was that the dominant hand had more sensory abnormalities than the non-dominant hand. This has not been reported in the general population. In our study, it was common to present with carpal tunnel syndrome or to have had a carpal tunnel release (45%) and we attribute this finding to greater sensory deterioration in the dominant hands of this group.

4.11.5 DEXTERITY

Dexterity has been described as having a peak, when aged in the early 20's, and declining with aging. Women have performed slightly better than men and the right hand has performed slightly better than the left (Kellor et al. 1971; Mathiowetz, Weber, et al. 1985; Oxford Grice et al. 2003). We found these small differences inconsistently. We believe that our study was underpowered for such small differences to reach statistical significance. In addition, there are more complex tests than the 9-hole peg test of dexterity that may be more suitable for testing differences in dextrous performance between the sexes or between the hands.

4.11.6 LIMITATIONS OF THIS STUDY

Our study had several limitations. Normative data was used for comparisons. However, grip strength has been tested in many samples of the general population

and the norms are robust. In contrast, the dexterity norms (Mathiowetz, Weber, et al. 1985) were developed with a homemade version that may give slightly different results to the Rolyan 9-hole peg test (Homecraft Rolyan, Notts, UK). The loss of dexterity may be a less reliable finding because of the assumption that the sets are similar.

The two year observation period was relatively short to detect longitudinal change. We detected a small sensory change that was statistically significant, but was not always clinically important. During this period, 20% of participants (n = 12) were lost to follow-up. Longer study duration may have allowed for greater deterioration in the study group and increased patient numbers may have increased the power of the study. These limitations are likely to underestimate changes but we do not believe they affect the overall conclusions.

4.11.7 SIGNIFICANCE OF THIS WORK

Despite these limitations, our study also had strengths. The data included a range of clinical variables and measured hand function broadly. Standardised instruments were used and appropriate statistical methods were applied to the different outcomes. We demonstrated that sensory function can deteriorate in the hand over a relatively short period of years. Hand function is rarely studied in diabetes, and our study has contributed to understanding the progression of sensory abnormalities.

4.12 Summary

- Our sample of adults with diabetes-associated hand disorders were characterised by:
  - Impaired grip strength
  - Impaired sensation
  - Functional limitations, decreased dexterity and hand symptoms
  - Poor physical health
- Sensory abnormalities occurred across the seven sites of the hand screen but occurred more frequently in areas supplied by the median nerve.
- Light touch perception deteriorated during a two year period.

- There were individual differences in sensory deterioration, with those individuals with trigger finger identified as having the greatest sensory loss.
- The dominant hand had a greater loss of sensation compared to the non-dominant hand.
- Other aspects of hand function remained stable during a two year period.

CHAPTER 5. ERROR AND BIAS IN OBSERVATIONS OF HAND FUNCTION

5.1 Introduction

Error and bias can be introduced into observations of hand function through various stages of a study. The sampling strategy, the choice of method of measurement, the standardisation of procedures and level of quality control in all aspects of data gathering and processing should be considered when assessing the validity of the results (Elwood 2007).

Clinical measures used for assessing the hands are relatively imprecise, which has implications when planning research for calculating sample sizes to ensure that research is adequately powered. Imprecise measures will increase the chance of making a type II error, or showing no difference when a real difference exists (Vandenbroucke et al. 2007).

Our hand assessment was designed around measures that were reliable and valid. We compared our results to normative data, analysed associations between different aspects of hand function and identified change. These different instruments were able to paint a broad picture of hand functioning in these disorders. There were moderate or weak associations between a person's functional difficulties, their health-related quality of life and the hand's impairments.

When our results were interpreted, the degree of error associated with the measured values and the significance of the observed change were considered. The error around estimates was conveyed by the width of the confidence intervals (CIs) or by the inter-quartile ranges that bounded these reported estimates. The magnitude of error associated with these measures increased the difficulty in detecting small changes during a two-year period. Despite this limitation, the scores from the hand sensation screen had sufficient precision to detect a small change in tactile sensation.

Our results can be used to calculate minimum detectable change when measuring hand function. The minimum detectable change is the smallest difference between two successive measures that can be expected to be greater than measurement error. Expressing the magnitude or error as a minimum detectable change using the original units of measure is designed to aid the clinical interpretation of an

individual's change. It is easier to interpret an individual's change as true change, rather than attributed to measurement error if it is greater than the minimum detectable change (Ferreira & Herbert 2008). There a number of variations on the name of this estimate, including the minimally detectable change (Beaton, Katz, et al. 2001; de Vet et al. 2006), the smallest detectable change (Ravaud et al. 1999), smallest detectable difference (Schreuders et al. 2003) or smallest real difference (Beckerman et al. 2001).

5.2 Rationale of study

Understanding sources of error or potential bias is important when conducting and interpreting the results of research. It is important for reducing their impact and may prevent the drawing of incorrect conclusions. The measurement error of our selected instruments is considered and interpreted in the context of our results. The meaning and importance of observed changes are discussed in more detail and the discrepancy between the calculated sample size and number recruited into our study is considered.

The aims of this chapter were to:

- determine minimum detectable change s for hand assessment measures
- suggest strategies to enhance the clinical interpretation of scores
- describe our strategies to recruit participants and reflect on their effectiveness

5.3 Methods

The analysis presents results from interpreting the data collected during the two year period of the study. Data from the assessment of grip strength, hand sensation, 9-hole peg test, and self-reported DASH scores are reported. Smallest detectable differences were calculated by comparing the amount of error associated with the difference between the first assessment and the second year of follow-up.

5.4 Statistical analysis

The magnitude of the change in grip strength, 9-hole peg test times or DASH scores required to detect a significantly significant change was determined by inspecting the average difference between the two assessments, the standard error of the difference and the 95% confidence intervals around the difference.

Minimum detectable changes (MDCs) were calculated from the standard error of measurement (SEM):

$$MDC = 1.96 \times \sqrt{2} \times SEM$$

The 1.96 derives from the 95% confidence interval and $\sqrt{2}$ is included because two measurements are involved in measuring change (Beckerman et al. 2001; Schreuders et al. 2003).

Alternatively, minimum detectable changes can be determined by examining 95% confidence intervals for the difference in measurements. A change between assessments larger than the 95% confidence interval of the difference could be considered indicative of a significant change 95% of the time (Nitschke et al. 1999).

When comparing our results with studies in which SEM was not reported, studies were identified from which the SEM could be calculated using the formula:

$$SEM = SD_{difference} \div \sqrt{2}$$

The standard error of measurement (SEM) is related to standard deviation of the change ($SD_{difference}$). It equals the standard deviation of the change ($SD_{difference}$) divided by $\sqrt{2}$ (Streiner & Norman 2003).

For the ordinal data from the examination of hand sensation, the minimum detectable change was estimated from the significant difference between the initial and two-year assessment, analysed with the Wilcoxon matched-pairs signed-ranks test.

The degree of correlation between different measures of change was used to assess the meaning of change. Spearman's rho was the correlation coefficient selected for the ordinal scale of the hand sensation screen.

5.5 Results

Four points was estimated as the minimum detectable change for the DASH questionnaire (table 5.1).

Two kilograms was estimated as the minimum detectable change for grip strength (table 5.1).

A change of 2 seconds in the average completion time was estimated as the minimum detectable change for the 9-hole peg test (table 5.1).

Table 5.1 Mean differences and minimum detectable changes between the initial and two-year follow-up for dexterity, grip strength and DASH scores

CI = Confidence Interval; SEM = standard error of the measurement; MDC = minimum detectable change

Variable	Observations	Difference (mean)	95% CI	SEM	MDC
9-hole peg test (sec)	48	-0.69	-1.73, 0.35	0.52	2 sec
Grip strength (kg)	48	-0.15	-1.6, 1.30	0.72	2 kg
DASH score (0-100)	46	0.80	-2.29, 3.90	1.53	4 points

Our result of a sensory change of 3 points, from a range of 35 points, was significant at $p = 0.03$. As this is close to the 95% confidence limit, we estimated that this was the minimum detectable change for the hand screen examining the peripheral nerve supply to the hand (table 5.2).

Table 5.2 Median scores, p-value and estimated minimum detectable change determined from sensory score (0-35) of the dominant hand.

MDC = minimum detectable change

Variable	Observations	Initial score (median)	2-year score (median)	p-value	MDC
Sensory score	48	25.5	23	0.03	3 points

5.6 Discussion

It was hypothesised that hand function would deteriorate slowly in our sample of adults with diabetes. At the start of the project, we considered which physiological measures and questionnaire assessments of the degree of functional limitation would best assess deteriorating hand function. At the end of the project, we re-evaluated the performance of our instruments used to measure changing hand function and considered the bias introduced by our study participants.

5.6.1 MINIMUM DETECTABLE CHANGE

Minimum detectable changes are an aspect of an instrument's reliability that assist in determining if a change has truly occurred or if it could be attributed to random error. We found minimum detectable changes for our hand assessment measures that were comparatively small. This is despite the expectation that longer time frames for carrying out repeated measurements are usually associated with a larger amount of variability (Guyatt, Kirshner & Jaeschke 1992). The smaller variability in our study may reflect that participants predominantly presented with chronic and stable conditions, or may reflect that observations were taken by one examiner, applying standardised methods in a consistent manner and with the same care to all.

We believe that maintaining a high level of quality control during data gathering and processing was one of our study's strengths and this would have reduced the error associated with our measures. Standardised procedures were followed for the hand assessments and a structured approach was used to facilitate collecting complete data for each participant. We distributed questionnaires prior to appointments, so that they could be completed beforehand, and forms were checked for completeness before the participant left from the hand assessment.

Occasionally, questionnaires were taken home following appointments and this resulted in increased workload following-up this data. Systematic checks for errors in the computer entry of all data were performed to ensure its accuracy and inconsistencies were checked from the originals. This was made easier as only one person (CR) had been involved in collecting the data.

The minimum detectable changes found in our study were compared with those from other studies. These have been reported for grip strength and for the DASH questionnaire.

5.6.2 DISABILITIES OF THE ARM, SHOULDER AND HAND QUESTIONNAIRE

Our estimate that 4 points was the minimum detectable change for the DASH questionnaire was relatively small. Prior estimates of minimum detectable change for the DASH have tended to be higher, for example, 11 points in a sample of hand osteoarthritis (MacDermid, J C et al. 2007) and 12.75 points in a range of upper limb conditions (Beaton, Katz, et al. 2001), which may reflect differences in the way these values are calculated. A similar value of 5 points has been previously reported but this estimate was calculated from one, rather than 1.96 times, the standard error of measurement (Szabo, R. M. 2001). We have shown that variability is not necessarily greater when participants are followed for a period of years, rather than weeks or months.

5.6.2.1 The meaning of scores

Because the meaning of individual scores is hard to interpret, clinicians rarely rely on them to identify problems or to monitor progress, preferring to ask patients directly what is wrong and if they are better (Jolles, Buchbinder & Beaton 2005). But, as clinicians gain experience in using the DASH questionnaire the meaning of different levels of disability may become clearer. Judgements may be able to made as to an individual's responses are lesser, greater or average for particular conditions (Jester et al. 2005). A judgment may be made as to whether responses are consistent with other aspects of an individual's presentation. Alternatively, individual scores can be compared to normative data or compared to data obtained from other samples of upper limb conditions (Jester, Harth & Germann 2005; MacDermid, J C et al. 2007). Our mean (95%CI) score of 25 (20, 30) at the

first assessment was significantly higher than normative values but lower than the mean (SD) scores of 34 (24) found in a sample of patients with wrist and hand problems (Beaton, Katz, et al. 2001) and 41(20) found in a sample of patients prior to surgery for carpal tunnel syndrome (Gummesson, Atroshi & Ekdahl 2003).

There are several limitations to DASH scores that may make interpreting the score more complex. Adaptive strategies that that individuals may use are not elicited, important difficulties may be overlooked (Bialocerkowski 2007) and higher scores have been attributed to musculoskeletal problems from other areas, such as the lower limb (Dowrick et al. 2006). Furthermore, difficulties performing activities that are self-reported, as measured by the DASH questionnaire, may differ from an individual's ability. What a person can potentially do is likely to differ from a person does in their usual environment because of factors such as the energy and time required or how socially important the activity is considered (Young, NL et al. 1996).

5.6.2.2 Determining attribution

Additional questions can be asked regarding difficulties with specific DASH items, with the aim of making these questions more specific by attribution (Amadio 2001). This could contribute insights into individual responses to particular questions. For example, one patient was asked, "Is it your shoulder or your hand that makes it difficult to wash your back?", with the answer that both areas contributed.

It is also worthwhile considering how individual's adapt, compensate and mange to use their hands for daily tasks. Supplementary questions can be asked to determine if important limitations have been overlooked and if adaptive strategies are being used. Clarifying responses with this level of detail has relevance for predicting how much change is likely following specific interventions.

Patients can also be encouraged to ask questions or add comments when completing the questionnaire. This will help determine if specific items are difficult to interpret or are less relevant for particular individuals. For example, item 21 that assessed difficulties with sexual function was the question that was most frequently unanswered in women (n=9, 26% of women). It was also the

question that was most frequently answered with a rating as unable in men (n=5, 19% of men). Our explanation for these divergent results is that this question was considered inappropriate or not applicable by some women, for example if someone was widowed, and assessed the effect of erectile dysfunction associated with diabetes in men.

5.6.3 GRIP STRENGTH

Our minimum detectable change of 2 kg for grip strength is less than the 6 kilograms previously found in women with non-specific pain (Nitschke et al. 1999) and it is less than the 6 kg found in men and 4 kg found in women in the general population (Young, NL et al. 1996). Strength can fluctuate on a day-to-day basis and varies in different populations, so the measurement error associated with grip strength found in one study should not be extrapolated to all patient populations. Because our measurements were relatively stable, the potential existed for a small change in strength to be detected in our sample.

5.6.4 DEXTERITY

We found that the variance associated with the 9-hole peg test was relatively small, so that a change of 2 seconds in the average completion time could potentially be detected. This small variance in the results was influenced by the proportion of individuals who completed the test easily. This test may not measure dexterity very sensitively, which may limit its use for evaluating the effectiveness of interventions (Mathiowetz, Weber, et al. 1985). Nevertheless, the time to complete tasks is worth studying, as we are all likely to make decisions about our ability to achieve based on the time and effort necessary to be successful (Backman et al. 1992)

5.6.4.1 Using serial measurements

Small changes in mean scores due to random change or a systematic effect are more likely to be statistically significant when variance is small (Streiner & Norman 2003). To manage this, serial measurements are recommended when using the 9-hole peg test in clinical studies with small sample sizes, as this will

minimise the likelihood of detecting small changes that could be significant but not clinically important (Beckerman et al. 2001; Streiner & Norman 2003).

5.6.4.2 Supplementing results with qualitative observations

Although the 9-hole peg test primarily generates a timed score, changes in movement quality when manipulating the pegs were observed in those with diminished tactile sensation. Pegs were frequently dropped as a consequence of difficulties gauging the grip force required to hold and manipulate the pegs. The method we followed recommended repeating the test if a peg was dropped. This resulted in participants with poor tactile sensation having repeated trials. One participant described the pegs, in Australian vernacular, as "slippery little buggers".

Interesting adaptive strategies were observed. One strategy was a quick double tap of the peg with the finger tips, quickly pinching, releasing and re-pinching the peg prior to lifting it. This may have been an adaptation to increase the sensory feedback used for gauging pinch grip strength. Another individual had changed their precision grip from the tripod pinch grip to the less efficient lateral pinch grip (fig 5.1). This was possibly a maladaptive strategy that could potentially change with feedback and training.

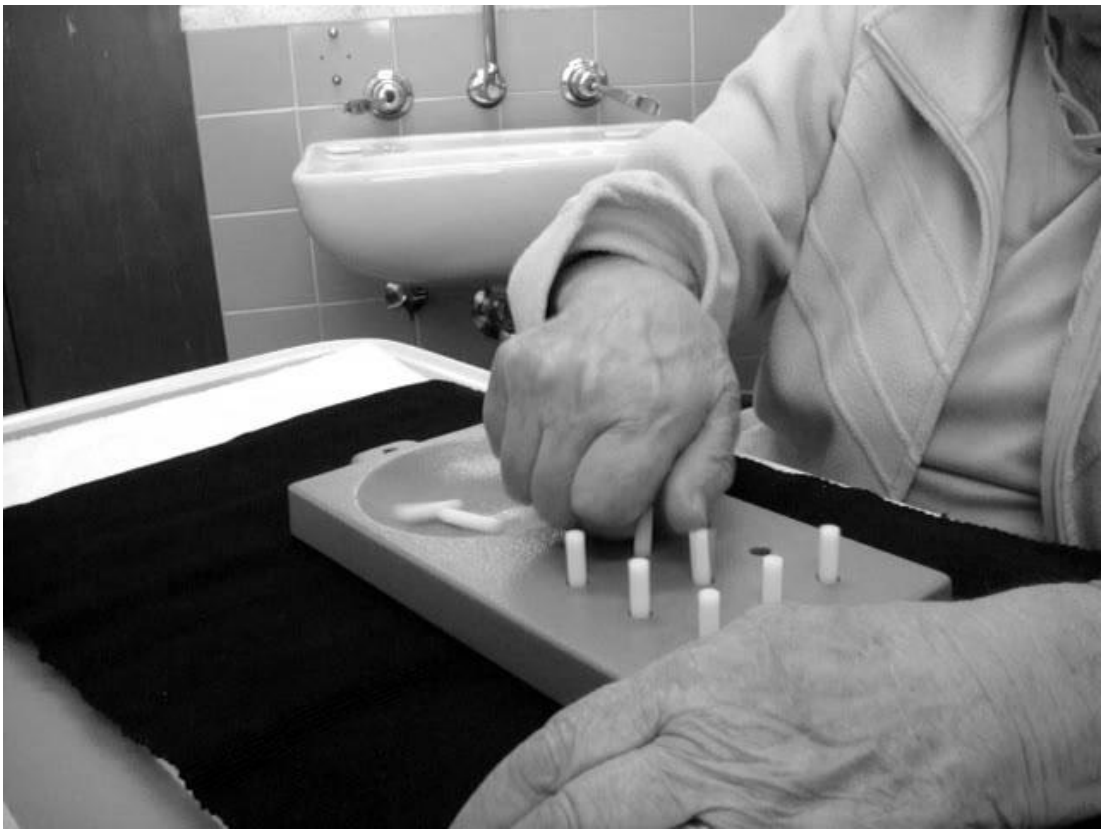

Figure 5.1 Lateral pinch grip being used to pick up a peg

5.6.5 TACTILE SENSATION

Our result of a change of 3 points, from a range of 35 points, was an estimate of minimum detectable change for the hand screen. We were confident that a real change had occurred but we were also interested if it was clinically important. The magnitude of change may differ between a minimally detected difference and a clinically important change (de Vet et al. 2006).

5.6.5.1 Interpreting clinical importance

To give an indication if there were clinically important consequences the relationship between the change in sensation and the change in dexterity was examined. The deterioration in tactile sensation was not significantly correlated with a change in dexterity (Spearman's rho = -0.21, p = 0.16). Our explanation of this result is that we detected an early deterioration of tactile sensation. Because it was a small loss, patients could adapt to it and dexterity was unaffected during the two-year period. Future research that follows patients for a longer period of time

is needed to assess the amount of sensory deterioration required to affect dexterity.

Future research could also investigate the underlying biological mechanisms for sensory deterioration in individuals with trigger finger. Ideally, Spearman's rho would have been used to assess the degree of correlation between the change in tactile sensation and change in nerve conduction velocities as well, if data were available.

5.6.5.2 Is a simplified test appropriate?

An additional consideration is whether it is necessary to test the seven points to screen the peripheral nerve supply to the hand. The hand screen that tested seven sites resulted in a good spread of data but it could be simplified, by testing less areas. It would seem plausible that evaluating tactile sensation to the finger tips are the most important areas to test in the hand screen as the finger tips are the contact points in fine manipulation.

Whether we tested the finger tips only or used the hand screen, our results would have been the same. A shortened sensory screen that tested the thumb, index and little finger tips would have detected the deterioration in tactile sensation as it occurred predominantly at the little finger tip. Testing only three finger tips may be an alternative and quicker test of tactile sensation that is useful in the clinic or for future research.

An early loss of sensation was detected but the detection of later sensory loss could have been limited by the increasingly coarse scale of the WEST hand monofilaments. This may be a particularly important when testing older adults who have age-related early sensory loss. The scale could be modified to a finer scale by adding one or two supplementary monofilaments. A future study could compare the sensitivity to change of the WEST hand set of monofilaments with a set with supplementary monofilaments that had a finer scale.

5.6.6 RECRUITMENT

Falling short in the rate of recruitment is one of the commonest problems in clinical research (Hulley, Newman & Cummings 2007). Recruitment took longer

than expected and did not meet the sample size requirements, which reduced the power of the study to detect change. The likelihood that differences fail to reach to reach statistical significance is increased when the sample is decreased.

Participants were recruited from hospital outpatient and private clinics. Ascertainment bias was introduced by the selection procedure as adults with diabetes-associated hand disorders tended to be selected if they had symptoms or were seeking treatment. Within the hospital, referrals were invited from clinicians and presentations about the study were given to medical and allied health staff in outpatients to inform staff about the study. Endocrinologists, orthopaedic surgeons, the diabetes educator, physiotherapists and podiatrists were included. Participating diabetic and orthopaedic clinics were regularly visited during the recruitment period to reinforce awareness that recruitment for the study was underway.

Our experience was that potential participants were identified by a small group of clinicians, which suggested that other clinicians missed potential participants. Hospital clinics are busy and time pressures on clinicians may have been a barrier to identifying adults presenting with a hand disorder, who also had diabetes, and vice versa. The importance of interested individuals who are supportive of research to success in recruiting has been previously noted. These individual clinicians who display enthusiasm for the project have been aptly described as "champions" (Borgiel et al. 1989; Ultee et al. 2003). Other strategies that were tried, but were ineffective, were using posters around the hospital, and advertising through hospital and local general practitioner newsletters.

Comparable studies investigating disability in diabetes-associated hand disorders have utilised different inclusion criteria and recruitment strategies (Cederlund et al. 2009; Savas et al. 2007), which has implications for generalising from each study's results. When reporting our results, we interpreted them within the overall context of these other studies, conducted in different settings and with different samples.

5.7 Summary

- The present study fills a gap in our understanding of the precision associated with methods measuring hand function when they are used during relatively long periods of follow-up.
- The standard errors of measurement around our results were examined to estimate the magnitude of change in these measures of hand function that would be genuine change 95% of the time.
- Minimum detectable changes for the 9-hole peg test of dexterity and for screening the hand's peripheral nerve supply using monofilaments were estimated.
- Minimum detectable changes that were relatively small were estimated for measuring grip strength and for using the DASH questionnaire. The measurement error in our sample was comparable to, or less than, the error previously found in other populations.
- Methods to assist with interpreting results include:
    - assessing the consistency of observations using serial tests over time
    - supplementing scores with qualitative observations
    - considering differences between minimum detectable change and clinically important change

CHAPTER 6. CONCLUSIONS

6.1 Introduction

Our aim of characterising disability in the hand disorders associated with diabetes was met. Impairments and reduced health-related quality of life were associated with these disorders and we demonstrated that sensory function could deteriorate, during a two-year period.

The role of measurement in clinical practice remains crucial. It has been central to collecting the prior evidence that suggests less favourable outcomes in patients with diabetes and will be central to further research aimed at developing strategies to ensure the best possible results in this population. Prior evidence that the presence of diabetes is an added challenge to optimal outcomes has been found for carpal tunnel syndrome, trigger finger and severe impairment in limited joint mobility (Baumgarten, Gerlach & Boyer 2007; Griggs et al. 1995; Haupt et al. 1993; Kiylioglu et al. 2009; Ozkul et al. 2002; Robertson, Earnshaw & Campbell 1979; Rozental, Zurakowski & Blazar 2008; Sibbitt & Eaton 1997; Stahl, Kanter & Karnielli 1997; Thomsen et al. 2009).

The increasing prevalence of diabetes has also driven more general research into the physical health consequences associated with its chronic complications and co-morbidities (Bruce, Davis & Davis 2005; Gregg et al. 2000; Gregg et al. 2002; Maggi et al. 2004). We have drawn upon this literature to support our observations that these hand disorders present in the context of poor physical health.

Obesity is a factor in the increasing prevalence of diabetes, has a negative impact on physical health (National Task Force on the Prevention and Treatment of Obesity 2000) and is a risk factor for carpal tunnel syndrome (Becker et al. 2002; Geoghegan et al. 2004). A challenge for health professionals is to what extent they engage with patients who have diabetes in managing their excess weight. Obesity negatively impacted upper limb function in our sample of adults with these hand disorders. It is a factor that needs to be addressed when managing poor physical health, muscle weakness and carpal tunnel syndrome.

In our day-to-day lives, objects are handled with either power or precision (Salter 2000). Hands require power for tasks requiring gripping, lifting and carrying and

precision for those tasks, such as writing, using keypads or handling small objects that require fine manipulation.

Factors that were potentially modifiable were identified. This has implications for future research and practice. Better outcomes may be achieved by addressing modifiable factors and improving capabilities of strength and dexterity in the hand. There is a need for clinical trials addressing exercise, and modifications to exercise required for patients with limited hand function. There is also scope to investigate the potential for hand care advice and access to adapted equipment to help patients to better manage their hand symptoms and difficulties.

6.2 Conclusions from this research

Diabetes-associated hand disorders were characterised by:

- increased difficulties completing daily activities
- reduced grip strength
- diminished light touch perception
- reduced dexterity, resulting in increased difficulties manipulating small objects
- poor physical health

Previous studies of adults with diabetes have found fewer difficulties with daily activities, in samples in which carpal tunnel syndrome and trigger finger occurred infrequently or were excluded (Cederlund et al. 2009; Savas et al. 2007). Our contrasting results suggest that difficulties with daily activities were predominantly associated with carpal tunnel syndrome and trigger finger.

Factors that are potentially modifiable and were related to disability were identified:

- Reduced grip strength, slowness completing the finger dexterity task and obesity independently predicted difficulties with daily activities.
- Aspects of physical and mental health independently predicted difficulties with daily activities.

A trend for the dominant hand to be stronger and more dextrous, previously identified in the general population, was evident to a variable extent in these hand disorders.

Sensory perception deteriorated slowly during a two-year period of follow-up. The median sensory loss was greatest in diabetic patients with trigger finger and in the dominant hand.

6.3 Recommendations for assessment

6.3.1 SCREENING FOR HAND DISORDERS

Our study showed that neuromuscular impairment was related to difficulties that individuals reported in performing everyday activities. Paying greater attention to complaints of hand symptoms, and identifying deteriorating strength, mobility or sensation at an early stage, when it is more easily reversed, may reduce the development of functional limitations. Screening for symptoms of pain and altered sensation affecting the hand could be incorporated into the care of patients with diabetes. If patients complain of characteristic symptoms, the hands can be examined for the diagnostic features of the different syndromes. Nerve conduction studies are an important additional investigation if symptoms are present that indicate carpal tunnel syndrome (Rempel et al. 1998).

6.3.2 MONITORING IMPAIRMENTS

We recommend clinically assessing impairments of strength and sensation. Monitoring grip strength using a dynamometer is a common clinical practice, and is considered relevant as there is evidence across many chronic conditions that strengthening can alleviate physical disability. In contrast, an assessment of tactile sensation using monofilaments is less routinely performed. This was a valuable assessment of the hand in diabetes as tactile sensation was necessary for manipulating objects with dexterity.

6.3.3 USING STANDARDISED QUESTIONNAIRES

We support recommendations to use appropriate outcome measures for impairments, activities of daily living and health-related quality of life (Amadio 2001; MacDermid, J C, Grewal & MacIntyre 2009; Wright 1999). Using questionnaires to measure the impact of a hand disorders on an individual's daily life has been inconsistently incorporated into clinical practice. We used a regional

questionnaire to assess upper limb disability and a health status questionnaire to assess the impact of these hand conditions and diabetes on health.

Poor hand function often co-existed with limitations of mobility and contributed to the presentation of poor physical health. The average values of the SF-36v2 in different domains demonstrated lower values for physical functioning, role limitations due to physical functioning, bodily pain and general health. Our findings contribute to prior research that diabetes is associated with physical limitations, obesity, depression and co-morbidities.

Measuring health status more rigorously could enhance our ability to predict the results of conservative or surgical management of these hand disorders in diabetes. Determining the contribution of psychosocial aspects and considering individual expectations and goals is central to a patient-centred approach to assessment (Vranceanu, Cooper & Ring 2009).

6.3.4 MEASURING DIFFERENT ASPECTS OF HAND FUNCTION

By measuring different aspects of hand function we were able to distinguish patients in whom weakness or loss of fine motor skills were important contributors to their functional difficulties and restricted their participation in work or leisure. Reference to norms that document age and sex differences in strength, sensory responses and dexterity, as well as differences between the right and left hands were useful aids in assessing a patient's departure from average values.

Our study supports the observations that measures of impairments and functional limitations are related but distinct (Wittink et al. 2003). The WEST monofilaments were more responsive to underlying physiological deterioration than the self-reported measures. This is in contrast to previous findings in intervention studies, in which self-reported measures were more responsive than impairment measures (Amadio et al. 1996; Katz et al. 1994). This reinforces that an instrument's ability to detect change is variable and should be interpreted in the context of the study's purpose and the population in which it is administered (Beaton, Bombardier, et al. 2001).

6.3.5 MEASURING OBESITY

Weight and height were measured to calculate BMI and we demonstrated that obesity in diabetes can have negative impacts on hand function. BMI does not directly measure body fat percentage or body fat distribution and other methods may be more accurate (National Task Force on the Prevention and Treatment of Obesity 2000). Despite this criticism, because a high BMI rating was an independent predictor of hand disability we recommend incorporating a clinical measure of obesity into hand assessments in diabetes. However, if treatment goals are to increase physical activity or healthy eating then more accurate measures of body fat may be chosen to evaluate success in achieving these goals.

6.4 Implications for measuring hand function

Our set of measures had limitations as well as strengths.

6.4.1 MEASURING GRIP STRENGTH

Measuring grip strength with a dynamometer was a useful measure for evaluating the relationship between impairment and disability. It had well-established procedures and extensive normative data.

6.4.2 MEASURING SENSORY PERCEPTION

Our study provided supporting evidence that individuals who were unable to detect the 0.07 gram and 0.2 gram monofilaments were likely to have poorer dexterity. Testing light touch with the WEST monofilaments was also able to evaluate deteriorating nerve function over successive annual assessments.

However, the ordinal scale was a limitation when the data was analysed. In addition, more extensive data on normative values and factors influencing the interpretation of values is required. More work is also required to refine techniques by comparing different procedures when applying the WEST monofilaments.

6.4.3 MEASURING DEXTERITY

The 9-hole peg test was a quick but limited test of dexterity and had normative data. These normative values were derived from a homemade pegboard, so

comparisons to this data should be interpreted cautiously. The Rolyan 9-hole peg test requires testing in the general population to further substantiate the original normative values. More recent data would also be valuable as increasing reliance on different technologies, such as computers, mobile phones and automated machines, may be changing daily activities and affecting the dexterity acquired in the population. Tools to evaluate dexterity more sensitively may be required to test this. The measurement of dexterity could be developed further by applying technology, similar to the motion sensors found in the Nintendo Wii.

6.5 Implications for further research and practice

Additional questions are also raised regarding the value of conservative measures to increase hand strength and improve dexterity. There is scope to evaluate specific conservative interventions in diabetic populations.

6.5.1 HAND STRENGTH AND FINE MOTOR SKILLS

Exercise strategies to improve the hand's strength and fine motor skills should be designed from our current knowledge of these conditions with the aim of reducing the associated functional limitations. We observed that pain inhibition and soft tissue contractures contributed to muscular weakness. Modifications to exercise may be required to minimise the risk of exacerbating symptoms associated with carpal tunnel syndrome, trigger finger or limited joint mobility.

The effectiveness of training on improving dexterity is also uncertain. Clinical trials could incorporate specifically training eye-hand coordination, using speed and accuracy, to improve dexterity. It is also possible that strength could contribute to dexterity, and clinical trials of upper limb resistance training to improve strength could evaluate this relationship.

The minimum detectable change associated with our assessments could be used when calculating a range of sample size requirements for clinical trials. While the amount of improvement for clinical importance is uncertain, it would need to exceed the measurement error associated with the instruments to be detected.

6.5.2 PHYSICAL HEALTH AND OBESITY

Addressing poor physical health and obesity has the potential to improve upper limb function. Clinical trials could be developed that evaluated general aerobic or resistance training compared to more specific upper limb exercises. Strategies to improve physical health may include advice and education on physical activity in diabetes and incorporate strategies to promote adherence to healthy activity.

There is also scope to evaluate precautions to exercise in diabetes and how best to monitor and manage the associated risk. Individuals in our sample had co-morbidities and musculoskeletal complications associated with diabetes that may have reduced their confidence in exercising safely.

6.5.3 CONSERVATIVE MANAGEMENT OF HAND DISORDERS IN DIABETES

New techniques and more specific strategies are being developed in the area of hand therapy with the aim of enhancing tendon and neural gliding (Lee, Nasser-Sharif & Zelouf 2002; Rozmaryn et al. 1998). These techniques could potentially be beneficial. Clinical trials of conservative management of these hand disorders in diabetes could evaluate:

- Strategies for limited joint mobility, which may include:
    - specific stretches and manual therapy to improve finger mobility
    - stretches and soft tissue techniques to improve muscle flexibility
    - using exercise with higher repetitions and lower resistance for improving muscle flexibility
    - advice on skin care to minimise the effects of diabetic skin changes, including increased skin dryness and splitting
    - finger massage to minimise oedema
- Strategies for trigger finger, which may include:
    - specific movements and massage to promote tendon gliding (Lee, Nasser-Sharif & Zelouf 2002)
    - modifying exercise or adapting activities to avoid repeated pressure to the palm or repetitive gripping (Ryzewicz & Wolf 2006)
- Strategies for carpal tunnel syndrome, which may include:

- specific tendon and nerve gliding exercises (Rozmaryn et al. 1998)
- advice on modifying or adapting activities to reduce symptoms (Burke et al. 2007; Lee, Nasser-Sharif & Zelouf 2002)

6.5.4 REHABILITATION FOR SURGICAL RELEASE OF TRIGGER FINGER

There is also scope to investigate strategies to enhance the outcomes from the surgical release of trigger finger, particularly when multiple fingers are involved, for example, in limited joint mobility. Prior to surgery, patients with preoperative finger stiffness and hand oedema could be advised on caring for their skin and instructed to perform active movements and massage. This pre-operative routine could be instigated with the aims of ensuring that the hand is in an optimal condition before surgery and familiarising the patient with postoperative expectations. Patients with pre-existing oedema are more likely to have further swelling and greater difficulty mobilising the hand in the postoperative period and require hand therapy.

6.6 Significance of this research

Health professionals may need to respond to and adapt their practice in response to burgeoning rates of obesity and type 2 diabetes. Hand conditions are common in diabetes, and when they are long-standing, severe impairment can result. If predictions on the rising prevalence of diabetes eventuate then it is likely that progressively more patients with diabetes and symptoms from carpal tunnel or trigger finger, in particular, will be seeking help from health professionals. Ongoing measurement of hand function remains important for making informed clinical decisions for individual patients.

Hand function in those with type 1 diabetes remains an area in need of further research. Assessing hand function in a younger sample may be beneficial in detecting the onset of changes to dexterity or strength.

A common aim of health professionals is to promote functional independence in their patients. Standardised methods are necessary for comparisons in order to distinguish individual responses, to document change over time and evaluate the effectiveness of treatment for these hand disorders.

The hand plays an essential role in our daily lives. Patients expect to use their hands for various daily tasks, across diverse occupational and recreational demands. Evaluating the effectiveness of our current approaches has the potential to change practice, leading to more effective strategies, and better results for individuals with diabetes. Adapting our practice may also be a necessary response to the challenges of managing the physical health of escalating numbers of adults with diabetes.

APPENDIX A PUBLICATIONS

Redmond, C.L., Bain, G.I., Laslett, L.L. and McNeil, J.D. (2009) Hand Syndromes Associated with Diabetes: impairments and Obesity Predict Disability.
Journal of Rheumatology, v. 36 (12), pp. 2766-2771, December 2009

APPENDIX B PRESENTATIONS

ORAL PRESENTATIONS

2010	Faculty of Health Sciences, Postgraduate Research Expo: Three Minute Thesis presentation
	Faculty of Health Sciences, Three Minute Thesis competition: Coming to grips with diabetes affecting the hands Redmond CL, Bain GI, Laslett LL, McNeil JD
2009	Australian Rheumatology Assoc (SA Chapter) meeting: Hand syndromes associated with diabetes: strength, dexterity and obesity predict disability. Redmond CL, Bain GI, Laslett LL, McNeil JD
2008	South Australian Hand Surgery Society Meeting: The impact of hand disorders associated with diabetes: relationships between functional difficulties and physiological impairments. Redmond CL, McNeil JD, Bain GI, Laslett LL
2007	Australian Physiotherapy Assoc Conference: Self-reported upper extremity disability and health status in adults with diabetes-associated hand disorders Redmond CL, McNeil JD, Bain GI, Laslett LL
	Australian Physiotherapy Assoc Conference: The impact of hand disorders associated with diabetes: relationships between self reported disability levels and physiological impairments Redmond CL, McNeil JD, Bain GI, Laslett LL
	Australian Rheumatology Assoc (SA chapter) Meeting: Upper extremity disability and health status in adults with the hand disorders associated with diabetes Redmond CL, McNeil JD, Bain GI, Laslett LL
2006	Australian Rheumatology Assoc (SA chapter) Meeting: Hand Function in Diabetes Mellitus: A pilot study Redmond CL, McNeil JD, Bain GI, Laslett LL

POSTER PRESENTATIONS

2008	Postgraduate Research Expo: Hand function in diabetes: influences of gender and obesity Redmond CL, McNeil JD, Bain GI, Laslett LL
2007	Postgraduate Research Expo: The impact of hand disorders associated with diabetes: Relationships between functional difficulties and physiological impairments Redmond CL, McNeil JD, Bain GI, Laslett LL

NOTE:
Appendices C, D and E are included in the print copy of the thesis held in the University of Adelaide Library.

To be part of this research please call Christine Redmond on 8161 2090.

What if I have a question about the study?

If you have any questions about the study, please contact Christine Redmond on ph: **8161 2090** or **0431 861 149**. Alternatively, you may contact her principal supervisor, A/Prof Julian McNeil on 8161 2090.

The Research and Ethics Committee, at the Modbury Public Hospital and the University of Adelaide Human Research Ethics Committee, have given approval for this study. If you wish to discuss aspects of the study with someone not directly involved, Catherine McKenna, the Secretary, Research and Ethics Committee, at Modbury Hospital may be called on 8161 2020.

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FACULTY OF HEALTH SCIENCES
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THE UNIVERSITY OF ADELAIDE
AUSTRALIA

RESEARCH INTO HAND FUNCTION AND DIABETES MELLITUS

Information Sheet

RESEARCH INTO HAND FUNCTION

Thankyou for considering whether you will be taking part in this research. Before agreeing to participate in the study, it is important that you read and understand the following explanation of the purpose of the study and procedures involved. This is a research project and you do not have to be involved. If you do not wish to participate or you wish to withdraw at any stage, your medical care will not be affected in any way.

What is the study about?
Diabetes mellitus is a disease that can cause damage to a number of body systems in the longer term. These complications can include involvement of the nerves and joints of the body. Over the last twenty or so years, there is increasing evidence that diabetes can affect the hands. The ability to use your hands for a variety of tasks is an important part of daily life. This aim of this research is to assess the impact of diabetic hand conditions on a person's ability to use their hands. This study is using questionnaires and a hand assessment to measure this disability. This knowledge may help health professionals assess and manage people with diabetes in the future.

What will the study involve?
You will be asked to participate in an assessment, which will involve one or two appointments. Appointments will take place in the Department of Medicine, University of Adelaide, located on the fifth floor of the Modbury Hospital. At the first session, you will be asked to complete three questionnaires: two that ask about your ability to perform activities and one on your general health. The researcher will also measure the movement in your hands, your hand strength and sensation. This procedure will take approximately an hour and a half. A second session may be required to complete the assessments.

Information on the severity of your diabetes and investigations for other diabetic complications will be found in your case notes. This information will be related to the presence of hand conditions and measures of hand function.

What happens to the information that is collected?
All personal information will be treated as strictly confidential. While information gained during the study may be published, no individual will be identified and personal results will not be divulged.

The completed questionnaires and data recording sheets will be kept securely in the Department of Medicine in accordance with University of Adelaide and Modbury Hospital research guidelines.

What are the risks, discomforts or inconveniences involved in the study?
There are no risks involved in the study. The hand assessment procedures are part of normal diagnosis and are generally not uncomfortable. There is small amount of inconvenience involved, from attending appointments.

What will I get out of the study?
The information gained will be used solely for the purposes of the study and no payment will be given for participation. Therefore, you will not directly benefit from the study. However, by participating you will be providing valuable information to assist in understanding the impact on hand function in individuals with diabetes.

Call 8161 2090

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