# Painful diabetic neuropathy:

# Exploring management options.

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## Abstract

Painful diabetic neuropathy (PDN) is one microvascular complication of diabetes mellitus (DM) and the focus of this thesis. PDN is a neuropathic pain condition characterised by severe burning pain in the feet and sometimes hands. It has significant impacts on peoples' mobility, sleep quality and overall quality of life. The personal and societal burden associated with DM and PDN is predicated to rise as prevalence rates increase.

Pharmacological management of PDN is often less than optimal, and people are left with few strategies to cope. Multidisciplinary pain management programmes (PMPs) use physical activity and psychological coping strategies to help people live better with persistent pain, yet people with PDN are rarely referred. It is unknown whether these strategies would be appropriate to help people live with PDN.

This thesis aimed to: 1) locate and appraise all literature relating to physical activity and psychological coping strategies in PDN; 2) interview people with PDN and explore how PDN impacted on their lives; 3) explore the perspectives of patients and clinicians on the relevance of PMP approaches; and 4) explore patients' treatment priorities and whether these might be addressed by PMP strategies.

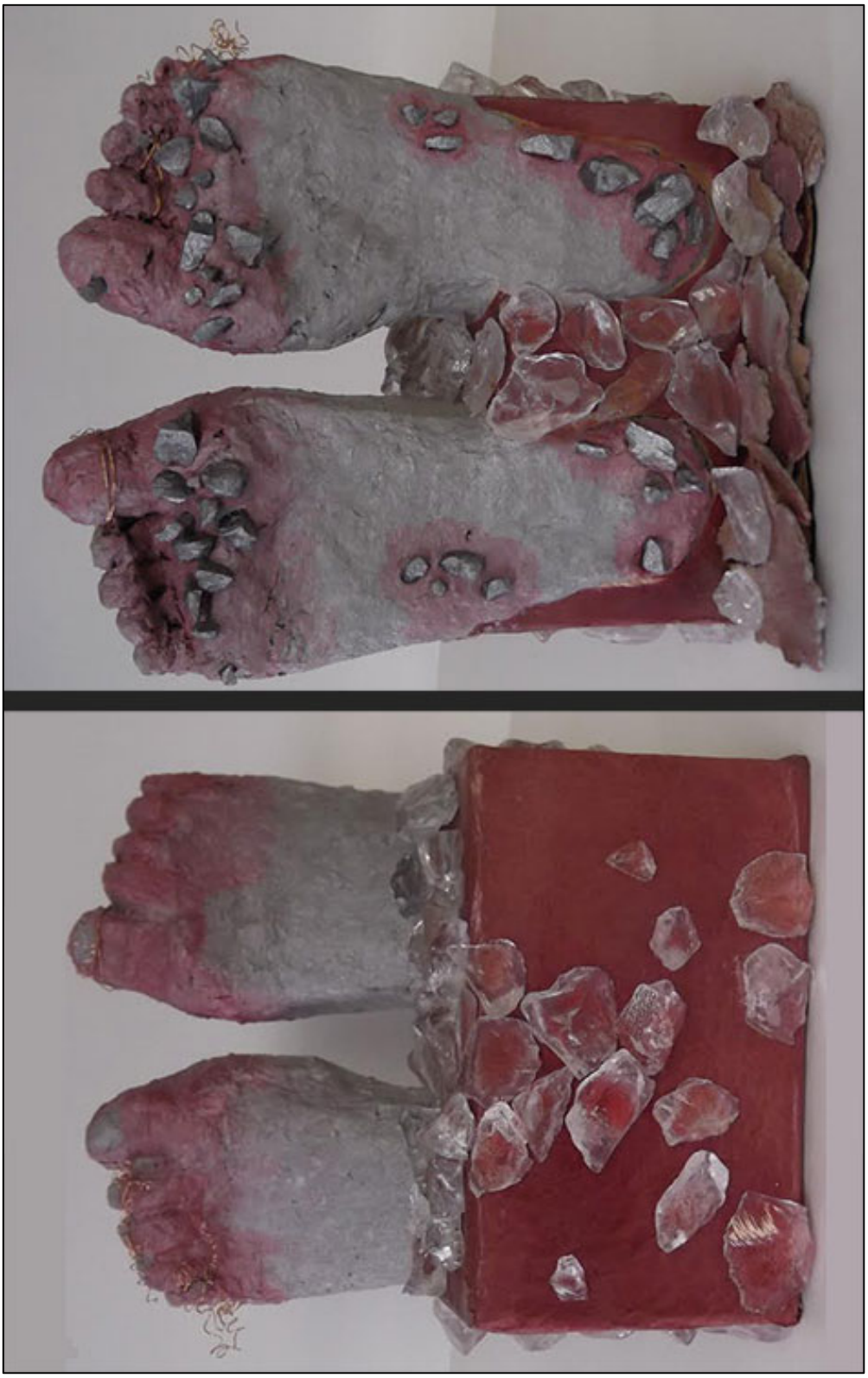
To address these aims, firstly a systematic literature review was conducted. The review identified a paucity of studies investigating physical activity or psychological coping strategies for PDN. Two interview studies were conducted, and data were analysed using thematic analysis (TA). A study with patients (n=23) found the impacts of PDN were wide ranging, people had experimented with many coping strategies unsuccessfully and there was some scepticism that PMP strategies were relevant to PDN, though few participants had direct experience of them. The second study interviewed specialist diabetes and pain clinicians and representatives from primary care (n=19). Clinicians relied primarily on medication strategies and did not have alternatives when these failed. Diabetes clinicians highlighted that people with PDN were medically complex patients and were at risk of tissue damage from too much physical activity. Pain clinicians felt PMP strategies could be adapted to suit the population with PDN.

Informed by the patient interview study, an Internet survey was developed to explore the management priorities of people with PDN (n=63 respondents). Sleep disturbance was the top priority in all subgroups analysed. There were six impacts most frequently prioritised by respondents, which did not include pain. Potential clinical management strategies for these impacts have been described, and suggestions made for future research.

This thesis has shown a scarcity of existing evidence for non-pharmacological strategies in the management of PDN. PMP strategies were not necessarily viewed as appropriate by patient participants. The impacts prioritized by people with PDN could however be matched to management strategies from other conditions where persistent pain is common. There is no *a priori* reason why these strategies could not be trialled with PDN. Managing the impacts of PDN on peoples' lives remains a complex process.

## Pain without words

Sculpture by Deborah Ann, who lives with painful diabetic neuropathy, from *Exhibiting Pain*. Reproduced with permission. www.exhibitingpain.wordpress.com



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A Doctorate in Philosophy is a significant undertaking, never embarked upon alone. This process has only been possible due to the continual love and support from Cerys and Daisy. Without them I would not have reached this point in the journey. Their patience has been immense and I hope I can repay them one day.

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Finally, I need to acknowledge the faith placed in me by my research supervisory team. I am aware I have not always thought or written like a researcher, but gradually you have all helped sculpt my thinking and writing to a doctoral level. Your critiques have always been spot-on and I could not be here without you all. Thank you to Professor David Wynick, Consultant Diabetologist, UHBT, who has acted as a clinical adviser on PDN and provided observations in his clinics. Thank you all, very much.

*Dedication*

My father Mervyn died in the middle of this doctorate. He had a life-long love of learning, gaining his BA (Hons) from the Open University when he had retired. For the loving support both my parents have given me from my earliest memory, I want to dedicate this thesis to them.

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## List of abbreviations

| | |
|---|---|
| ACT | Acceptance and Commitment Therapy |
| BMI | Body mass index |
| BPCI-2 | Brief Pain Coping Inventory-2 |
| BPI | Brief Pain Inventory |
| BTX-A | Botulinum toxin-A |
| CAQDAS | Computer Assisted Qualitative Data Analysis Software |
| CBT | Cognitive Behavioural Therapy |
| CBT-I | Cognitive Behavioural Therapy for Insomnia |
| CI | Confidence Interval (95%) |
| COREQ | Consolidated criteria for Reporting Qualitative research |
| CSQ | Coping Strategies Questionnaire |
| DALYs | Disability Adjusted Life Years |
| DM | Diabetes Mellitus |
| DPNPI | Diabetic Peripheral Neuropathy Impact measure |
| DSN | Diabetic Specialist Nurse |
| DUK | DiabetesUK |
| EBM | Evidence based medicine |
| EPRP | Expert patient research partner |
| EQ5D | EuroQoL health outcome questionnaire |
| FMS | Fibromyalgia syndrome |
| GP | General Practitioner |
| HADS | Hospital Anxiety and Depression Scale |
| HbA1c | Glycated haemoglobin level |
| HCP | Health care professional |
| IBS | Irritable Bowel Syndrome |
| ICD-10 | International Statistical Classification of Diseases and Related Health Problems |
| IPA | Interpretative Phenomenological Analysis |
| IQR | Interquartile range |
| LBP | Low back pain |
| MBSR | Mindfulness-based stress reduction |
| MDT | Multi-disciplinary team |
| MOM | Mature Organism Model |
| MOS | Medical Outcomes Sleep survey |
| MS | Multiple Sclerosis |
| NICE | National Institute for Health and Clinical Excellence |
| NHS | National Health Service |
| NNT | Number needed to treat |
| NRS | Numerical rating scale |
| NeuroQOL | Quality of life for neurological diseases |
| OR | Odds Ratio |
| PCA | Principal component analysis |
| PDN | Painful diabetic neuropathy |
| PHN | Post-herpetic neuralgia |

| | |
|---|---|
| PHQ-9 | Patient Health Questionnaire-9 |
| PIS | Participant Information Sheet |
| PMP | Pain management programme |
| PNS | Parasympathetic nervous system |
| PPP | Peak plantar pressure |
| PsyCS | Psychological coping skills |
| PRIMSA | Preferred Items for Systematic reviews and Meta-analysis |
| QALYs | Quality Adjusted Life Years |
| QOF | Quality Outcomes Framework |
| RCT | Randomised Controlled Trial |
| RR | Relative risk |
| SD | Standard Deviation |
| SF36 | 36-item Short Form Health Survey |
| SMD | Standardised mean difference |
| SNS | Sympathetic nervous system |
| T1 or 2 | Type 1 or 2 diabetes |
| TA | Thematic Analysis |
| TDI | Thompson Deprivation Index |
| THC | Tetrahydrocannabinol |
| UK | United Kingdom |
| USA | United States of America |
| VAS | Visual Analogue Scale |
| WHO | World Health Organisation |
| WHYMPI | West Haven Yale Multidimensional Pain Inventory |

# Chapter 1 – Introduction

*This thesis explores the experience of people who live with painful diabetic neuropathy (PDN), a microvascular complication of diabetes mellitus (DM). It investigates how PDN impacts on their lives and how they, and clinicians involved in their healthcare, currently manage these impacts. It explores whether management strategies used with other persistent pain conditions might be acceptable adjuncts to management of PDN and associated impacts. Lastly, the thesis investigates which impacts patients prioritise to manage more effectively and places these in the context of existing evidence.*

*This chapter will give a background to diabetes as a chronic health condition and highlights the range of complications that can occur. It will introduce PDN as one of these complications, and describe what is currently known about the impact of this condition on peoples' lives. Lastly, it will outline the aims of this thesis, the research questions, and the thesis structure.*

## *1.1 Diabetes Mellitus*

Diabetes Mellitus (DM) is an endocrine disorder characterized by maintained hyperglycaemia (raised blood sugar level) due to loss of insulin secretion and/or impairment of insulin sensitivity at the target tissues (Holt and Hanley, 2012a). In 1999 the World Health Organisation (WHO) revised the classification of types of diabetes; Type 1 DM (T1DM) is an autoimmune disorder that leads to the destruction of β-cells within the pancreas; this tends to be diagnosed in childhood or adolescence. The loss of β-cells abolishes all insulin secretion and requires lifelong management with insulin replacement therapy. Type 2 DM (T2DM) is the result of depleted insulin secretion by β-cells and/or resistance to the action of insulin at target tissues. T2DM tends to be diagnosed later in life. Other diagnoses include diabetes secondary to other endocrine or pancreatic disorders, specific genetic mutations, or pregnancy (Holt and Hanley, 2012b).

### *1.1.1 Historical perspective*

Diabetes has been recognised as a clinical phenomenon within Egyptian (~1500 BC), Indian (5th Century BC) and Greek (2nd Century AD) medical texts. The Persian physician Avicenna (980-1037 AD) described the altered appetite, sweet tasting urine, propensity for gangrene and impotence that affected people with diabetes. Diabetes takes its name from the Greek *diabainein*, meaning "to pass through", in relation to the volume of urine people with diabetes can produce. In the 18th Century, the term Diabetes Mellitus (honey) was used to differentiate patients with sweet tasting urine, from patients whose urine was tasteless or insipid (Holt and Hanley, 2012a; Kumar, Kumar and Janardan, 2013). At the end of the 19th Century the pivotal role of the pancreas and specifically the β-cells were demonstrated. β-cells, also called Islets of

Langherhans, are cells that release insulin into the portal vein in response to a meal. The function of insulin was discovered in 1921 by Sir Frederick Banting and John MacLeod and its structure was demonstrated in 1955 by Frederic Sanger.

The purification of insulin and its emerging therapeutic use in the 1920s and onwards was revolutionary in the treatment of T1DM. Sir Frederick Banting and Charles Best did not patent their process for the production of insulin nor try to restrict the commercial application of its use. From a condition that would lead to weight loss and death within weeks to months, the survival time was increased to years and then decades. Insulin therapy has developed from using bovine insulin in 1923, to using recombinant DNA techniques to sequence and produce human analogue insulin in the 1980s.

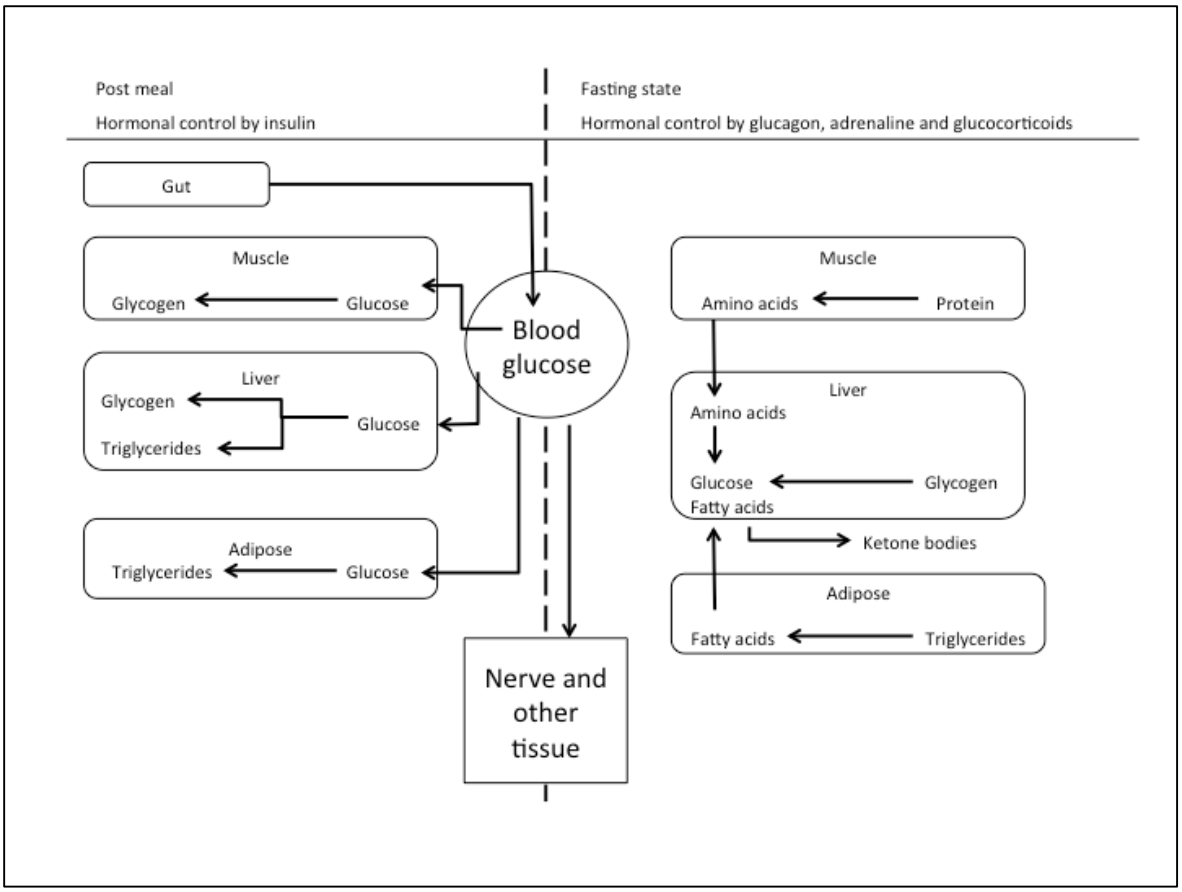
Research continues into the optimisation of insulin delivery. This research includes different analogues of insulin with pharmacokinetic properties that mimic the physiological release profile of functioning β-cells, the development of an external pancreas that can continually monitor blood glucose levels and deliver insulin appropriately, and the transplantation of both pancreas and β-cells into the patient with diabetes (Holt and Hanley, 2012a; Lawton *et al.*, 2015).

### *1.1.2 Functions of the pancreas and the role of insulin*

The pancreas is located in the abdomen and sits at the outflow of the stomach at the duodenum. As an exocrine gland, it delivers digestive enzymes directly into the duodenum to aid with the digestion of protein, carbohydrate and fat within the food ingested. As an endocrine gland, it secretes hormones directly into the blood flow that passes through its capillary bed. Cell subtypes within the pancreas have different roles: α-cells secrete *glucagon*; this hormone increases glucose concentration in the circulation. β-cells secrete *insulin*; this decreases the circulating blood glucose concentration. It is the secretion of insulin and the subsequent effect at target tissues that is of most relevance to the pathophysiology of diabetes (Inzucchi *et al.*, 2012).

The β-cells release insulin at a basal rate, which accounts for approximately 50% of the insulin released over a 24-hour period. Immediately after a meal is eaten there is an early rapid insulin secretion phase followed by a sustained insulin secretion phase. The insulin is released into the pancreatic capillary beds which develop to form the hepatic portal vein. The hepatic portal vein transports the insulin directly into the liver tissue where it has a primary site of action (Kahn, Cooper and Del Prato, 2014).

Figure 1 - Regulation of blood glucose concentration *adapted from* Holt & Hanley (2012) *(reproduced with permission)*




The actions of insulin are manifold and complex (partially summarised in Figure 1). Insulin binds to a range of different target cells and has different effects depending on cell type. Insulin impacts on carbohydrate metabolism by causing glucose to be taken up from the circulation into the cells; it facilitates glycogen synthesis and inhibits both glycogen breakdown and gluconeogenesis (creation of glucose from non-carbohydrate sources). Insulin modulates the metabolism of fatty acids by facilitating the formation of triglycerides and cholesterol, whilst inhibiting their breakdown. Insulin is also involved in protein metabolism by increasing the uptake of amino acids and promoting protein synthesis (Inzucchi *et al.*, 2012). These actions occur in all cells in the body although the majority of these effects occur in the liver, the concentration of insulin in the blood stream leaving the liver can be decreased by up to 40%. The actions of insulin are modified and modulated by the synergistic actions of many other hormones including glucagon, adrenalin, and glucocorticoids. It is regulated by the relative neural activity of the sympathetic nervous system (SNS) and parasympathetic nervous systems (PNS). Finally, insulin release is affected by behavioural and social factors such as exercise (Petersen and Pedersen, 2005) and stress (Lasselin *et al.*, 2012).

*1.1.3 The pre-diabetic state*

The pathophysiological processes of reduced release and action of insulin can exist without overt symptoms for many years. This has been termed a pre-diabetes state (Horowitz, 2006). As the effect of insulin at target tissues declines, β-cells increase the rate of insulin release (hyperinsulinemia) in order to maintain blood glucose levels within a physiological range (euglycaemia). With continued tolerance to insulin action a state of hyperinsulinemia and hyperglycaemia is reached, which eventually progresses to β-cells depletion and a loss of insulin secretion (hypoinsulinemia), and maintained hyperglycaemia (Donahue and Orchard, 1992). This state can exist for a prolonged time before possibly leading to signs and symptoms that would be diagnosed as diabetes. Alberti and Zimmet (2013) estimated that 20-25% of people with T2DM in the United Kingdom (UK) are undiagnosed.

*1.1.4 Diagnosis of diabetes*

The diagnosis of DM has been informed by two abnormal plasma glucose concentrations, following an oral glucose tolerance test or an eight-hour fasting state (Bennett, Guo and Dharmage, 2007). Fasting glucose tests have low sensitivity (mean 0.25 (Confidence Interval (CI) 0.19 to 0.32)) so are prone to false-negative results, but high specificity (mean 0.94 (CI 0.92 to 0.96)) (Barry *et al.*, 2017). Glucose tolerance tests are relatively costly to administer and can be affected by technique and laboratory variables (Bennett, Guo and Dharmage, 2007). To account for false negative rates, diagnosis of diabetes was based on a combination of results, see Figure 2 below (Holt and Hanley, 2012a).

Figure 2 - World Health Organisation diagnostic criteria for diabetes, 1999 (Holt and Hanley, 2012a) *(reproduced with permission)*

| | | **Fasting plasma glucose** | | |
|---|---|---|---|---|
| | | <6.1 mmol/L | ≥6.1 – 6.9 mmol/l | ≥7.0 mmol/L |
| **2h plasma glucose following 75g oral glucose tolerance test** | <7.8 mmol/L | Normal | Impaired fasting glycaemia | Diabetes |
| | ≥7.8 – 11.0 mmol/L | Impaired glucose tolerance | Impaired fasting glycaemia *and* impaired glucose tolerance | Diabetes |
| | ≥11.1 mmol/L | Diabetes | Diabetes | Diabetes |
| *The American Diabetes Association defines impaired fasting glucose as 5.6-6.9 mmol/L Diabetes may also be diagnosed if random plasma glucose is ≥11.1 mmol/L* | | | | |

More recently the diagnostic process has included measurement of glycated haemoglobin levels (HbA1c) (Kilpatrick, Bloomgarden and Zimmet, 2009). Glucose in the blood plasma binds irreversibly to haemoglobin molecules until the body reabsorbs the erythrocytes. The concentration of plasma HbA1c increases proportionally to plasma glucose so giving an insight to blood glucose concentrations across 2-3 months, the lifetime of the erythrocytes (Bennett, Guo

and Dharmage, 2007). The WHO, the International Expert Committee and the American Diabetic Association now define HbA1c of ≥6.5% (≥48mmol/mol) as diagnostic of diabetes and HbA1c 5.7-6.4% (40-47 mmol/mol) as indicating a raised risk of developing DM (Holt and Hanley, 2012a; Barry *et al.*, 2017).

There are efforts to improve the early detection of diabetes and implement appropriate treatments so that associated costs of the disease might be mitigated and reduced, for both the person and health systems. Current NHS cost estimates for diabetes are £23.7 billion and this is expected to rise toward £39.8 billion by 2035-36 (Barry *et al.*, 2017). A recent systematic review evaluated the evidence to establish whether diabetes pre-screening programmes were useful for identifying people who did go onto develop DM (Barry *et al.*, 2017). The authors used oral glucose tolerance tests (fasting glucose and glucose tolerance tests as described in Figure 2 above) as gold standard for diagnosing pre-diabetes glycaemic results and compared HbA1c data to assess its predictive value. HbA1c was found to have a sensitivity of 0.49 (CI 0.40 to 0.58) and specificity of 0.79 (CI 0.73 to 0.84) for diagnosing prediabetes in line with oral glucose tests (Barry *et al.*, 2017). The moderate results of specificity and sensitivity mean people might be reassured they do not have an increased risk for diabetes when they do (false negative), or referred for treatment when they do not require it (false positive).

*1.1.5 Epidemiology and risk factors*

In the UK, the population prevalence of diabetes was reported at 6% (DUK, 2012a), which equated to 3.2 million adults. Data from 2009 indicated a lower prevalence of 5.1%, suggesting prevalence is increasing (DUK, 2010). A similar increase has been noted globally (Inzucchi *et al.*, 2012). The majority of adults with diabetes have T2DM (90%), with 10% having T1DM (NICE, 2015b). Of the adults with T2DM, 56% are male and 44% female. The presence of pre-diabetic states means people can have episodes of hyperglycaemia, without demonstrating clinical symptoms that would lead them to health services. The majority of children with diabetes have T1DM, although diagnosis of children and adolescents with T2DM is increasing (DUK, 2012a).

Type 2 DM has higher prevalence in Black and Minority Ethnic groups, particularly people from South Asia compared to rates in Caucasians. Diabetes prevalence in India and Bangladesh are 8-10% (Gujral *et al.*, 2013). People with a South Asian background tend to develop resistance to insulin action at a younger age, and are predisposed to have higher amounts of abdominal and visceral fat even for matched body mass index than Caucasian populations (Gujral *et al.*, 2013).

There are social and demographic risk factors known to increase the risk of developing T2DM. The balance between energy intake and energy expenditure has gradually changed in recent decades in Western societies, as calories have become cheaper and modern society

demands less physical activity. This shift has led to an increase in the population percentage classed as obese and heavier. There have been cultural shifts in diet toward pre-packaged and processed foods that often contain higher proportions of sugar and fat. A raised intake of calorie-dense food can lead to an increase in percentage body fat composition. Episodes of life stress can be associated with less-healthy choices of diet and consequent increases in circulating inflammatory markers (Alford, 2006; Kiecolt-Glaser, 2010). The deposition of adipose tissue around the abdomen has been linked to the pre-diabetes state (Eckel, Grundy and Zimmet, 2005).

Behavioural factors such as smoking and coffee consumption have been shown to alter the risk of developing diabetes. Light smokers have a relative risk (RR) of 1.29 (CI 1.13 to 1.48 and heavier smokers (≥20 cigarettes/day) an RR 1.61 (CI 1.43 to 1.80) of developing T2DM (Willi *et al.*, 2007). In contrast to tobacco, caffeinated coffee consumption has been associated with reduced risk of DM. Conversely, high coffee consumption (≥7 cups/day) had RR 0.65 (CI 0.54 to 0.78) when compared to low coffee consumption (0 to ≤2 cups/day) (van Dam and Hu, 2005).

Sedentary behaviours, particularly prolonged sitting and screen time, in childhood have been associated with increased risk of cardiovascular diseases and diabetes at 30 years of age (Department of Health, 2010a). National and International guidance suggest 150 minutes of 'moderate exercise' each week are required to offset health risks of sedentary lifestyles (Sparling *et al.*, 2015). Moderate intensity walking or cycling is defined by the level of breathlessness caused; where conversation is limited to short sentences, this is seen as 'moderate exercise'.

Social factors mediate the development of diabetes. Perceptions of more difficult childhood experiences have been associated with increased prevalence of diabetes (Tomasdottir *et al.*, 2015). Living in a deprived urban area is associated with increased risk of diabetes compared to more affluent suburbs that are only a short distance removed (Steno Diabetes Center/UCL, 2016). These social factors can be considered as stressors on the physiological system, which then responds with a variety of hormonal cascades including adrenaline, cortisol and pro-inflammatory biomarkers. These agents all have an impact on the control of blood glucose levels (Tsigos and Chrousos, 2002; Chrousos, 2009).

In summary of section 1.1.5, development of diabetes has been shown as multi-factorial, with development of the disease state dependent upon a wide range of factors including genetics, diet, activity levels, smoking, life stress and social environment.

*1.1.6 Impact of diabetes*

Diabetes has significant negative impacts on quality of life. A global review of Disability Adjusted Life Years (DALYs) demonstrated an increase in diabetes-associated disability from 27,706 DALYs in 1990 (global estimate for one year, all ages) to 46,823 in 2010, an increase of

69%. In 1990 diabetes was ranked 21st in all diseases and had risen to 14th by 2010 (Murray *et al.*, 2012). The increase in DALYs was due to both rising prevalence rates of DM and improved treatment. Better treatment has reduced mortality but increased the number of people living long-term with the disease and its consequences (Alberti and Zimmet, 2013).

Large-scale studies have investigated the symptom burden of DM. Sudore *et al.* (2012) conducted a survey with people diagnosed with DM (n=20,188, 62% response, n=13,171 cases included). Of the sample (mean age 60.0 years (SD9.9), 47% female, mixed ethnic backgrounds), 39.7% experienced persistent pain, 23.8% experienced sensory loss due to diabetic neuropathy, 24.2% experienced sleep disturbance and 23.5% were depressed (Patient Health Questionnaire-9 (PHQ-9)) (Sudore *et al.*, 2012).

Depression and anxiety are reported as more common amongst people with DM than matched controls. A postal survey of people with T1 and T2DM (n=1456, response rate 71%) found 22.4% of respondents (CI 20.2 to 24.7%) were classed with mild to severe depression (general population prevalence 10.4-11.2%) and 32% (CI 29.5 to 34.6%) were classed with mild to severe anxiety (general population prevalence 15.3%) (Collins, Corcoran and Perry, 2009). Anxiety has been studied less frequently than depression. A retrospective data base study (total n=201,575, n=20,142 with DM) showed the lifetime risk of anxiety to be 19.5% in people with DM and 10.9% in matched controls without DM. After adjustment for other sociodemographic variables, the DM cohort were 20% more likely to be diagnosed with anxiety (prevalence ratio 1.20, CI 1.12 to 1.30) (Li *et al.*, 2008).

There is some evidence that DM has an impact on cognitive function in later adulthood and potentially that DM maybe a factor in the development of Alzheimer's disease (RR 1.5-2.0) and vascular dementia (RR 2.0-2.5) (Biessels, Deary and Ryan, 2008). Biessels *et al.* (2008) acknowledge cognitive performance declines with age but highlight that episodic hypoglycaemia and stress at crucial periods of life, especially early childhood, have been implicated in advanced rates of cognitive decline in later life.

Prolonged episodes of hyperglycaemia can lead to inflammation in the epithelial lining of the vascular system and release of free-radicals (Shakher and Stevens, 2011). With prolonged exposure to these inflammatory mediators diabetic neuropathy can develop. Diabetic neuropathy (without pain) is characterized by loss of sensory and nociceptive information (feet insensate to damage), a decline in proprioceptive reactions, increase in standing balance sway and risk of falls (van Schie, 2008). Presence of neuropathy has been associated with reduced physical mobility on the Nottingham Health Profile physical mobility scale. The risk of ulceration and consequent amputation is increased with neuropathy; careful foot assessment and self-care are vital to

mitigate this risk (NICE, 2015b). Clinical foot assessment includes vibration sense test (128Hz tuning fork), monofilament tests (10g Semmes-Weinstein) and possible use of a range of screening questionnaires, for example the Neuropathy Symptom Score (Lavery, Armstrong and Boulton, 2004) or Leeds Assessment of Neuropathic Signs and Symptoms (Bennett *et al.*, 2005). These foot assessment procedures are currently recommended by National Institute for Health and Clinical Excellence (NICE) (NICE, 2015b), DiabetesUK (DUK) (DUK, 2012b) and are part of the Quality Outcomes Framework (QOF) for UK primary care clinicians (NHS Employers, 2016).

Lastly, diabetes is associated with increased incidences of common musculoskeletal conditions. Adhesive capsulitis has an incidence of 2-10% in the population without diabetes rising to 11-20% in the population with diabetes. Dupuytren's contracture, a thickening and shortening of the flexor tendons in the palm has an incidence of 13% in the population without diabetes rising to 20-63% in people with diabetes (Smith, Burnet and McNeil, 2003).

In summary of section 1.1.6, the consequences of diabetes are complex and inter-related. Depression, anxiety, altered sleep pattern, altered mobility, altered circulating inflammatory markers and on-going stress from managing a long-term condition are not only consequences of diabetes, but have the potential to negatively affect the person's ability to self-manage their condition. The following section will detail the strategies that are important for optimum management of diabetes, both from the clinicians involved and from the person.

### *1.1.7 Management of diabetes*

Type 1 DM involves autoimmune destruction of β-cells, which may ultimately lead to complete abolition of insulin secretion. Treatment for T1DM involves insulin therapy, in addition to appropriate lifestyle modification and dietary advice, from a much earlier point in the diagnostic and management journey (Holt and Hanley, 2012a). In contrast, T2DM is managed with a combination of diet and lifestyle advice, with medications if required. This spectrum of clinical presentation ranges from early diagnosis of T2DM being successfully managed by diet and lifestyle changes with no need for medication, to the other extreme where continual loss of β-cells, and hence insulin, may then require insulin therapy.

Current NICE guidance focuses on five key principles of DM management: (1) patient education, (2) dietary and activity advice, (3) blood pressure management, (4) blood glucose management, and (5) appropriate drug management (NICE, 2015b). Education is critical to maximise patient engagement in self-management of diabetes. Education is targeted at family and partners in addition to patients, because social support networks have been shown as beneficial in managing long-term conditions (Strom and Egede, 2012).

There are currently some differences in the dietary advice given by the National Health Service (NHS) and by DUK. They give similar advice to eat regular meals (not skip meals), eat at least five portions of fruit and vegetables daily, increase dietary fibre intake, limit salt and alcohol, choose lean meat, fish, eggs and pulses as sources of protein and keep hydrated with water (DUK, 2017; NHS, 2017). The NHS advises eating plenty of complex carbohydrates (whole grain pasta and bread) with low glycaemic index; pure glucose has a glycaemic index of 100 with low defined as ≤55. DUK recommend 'counting' carbohydrates to ensure a closer monitoring of consumption.

Lifestyle advice also encourages physical activity. The minimum recommended level of activity (150mins/week, moderate intensity) has been discussed in section 1.1.5. This guidance is for reducing the likelihood of developing a range of health conditions, so not specific to diabetes, but has been endorsed by diabetes organisations (Nagi and Gallen, 2010). This activity can reduce the risk of developing complications associated with diabetes, such as cardiovascular disease (Nagi and Gallen, 2010).

A systematic review included eight studies and found improved diet and physical activity levels reduced the relative risk of developing diabetes by 37% (RR 0.63 (CI 0.49 to 0.79) (Orozco *et al.*, 2008). There were associated reductions in waist circumference (a measure of abdominal fat deposition), body weight and blood pressure. Increasing physical activity has been shown to have association with reductions in HbA1c (7.65% vs. 8.31%, mean difference -0.66%, $p<0.001$) when compared to control arms (Boulé *et al.*, 2001). Boule *et al.* (2001) excluded studies including drug interventions in order to remove the confounding effect of medication. There was no significant change in body mass (83kg vs. 82.4kg, mean difference 0.54, $p=0.76$) between the intervention and control arms (Boulé *et al.*, 2001). This review highlighted that the physiological benefits of exercise can be attained in the absence of weight loss.

NICE advocate regular monitoring of blood pressure in people with DM and the use of anti-hypertensive drugs where necessary to achieve normotensive pressure (NICE 2015). Uncontrolled hypertension has an increased risk of cardiovascular disease, cerebrovascular accidents and nephropathy (Donahue and Orchard, 1992). Hypertension within neural capillary beds also predisposes towards further microvascular damage and consequent neuropathy and retinopathy (Tooke, 1995).

Management of blood glucose levels is a key principal of management. Hypoglycaemia (low blood glucose) will lead to cellular energy supplied by alternative biochemical pathways. These pathways use beta-oxidation releasing ketone bodies that are toxic. Increasing ketone concentrations lead to vomiting, abdominal pain, confusion and loss of consciousness. Conversely hyperglycaemia (high blood glucose) leads to increased rates of free radical release, epithelial cell

inflammation and consequent microvascular changes. Current guidelines aim for an optimum target HbA1c of 48mmol/mol (6.5%), or 53mmol/mol (7%) if taking medication associated with hypoglycaemia (NICE, 2015b).

*1.1.8 Complications of diabetes*

In section 1.1.6 the impacts of diabetes were outlined. These included higher rates of pain, depression, anxiety, cardiovascular diseases and declines in cognitive and balance functions when compared to a population without diabetes. When diabetes is not optimally managed, a range of complications become more likely. These can be divided into two types: 1) macrovascular complications leading to cardiovascular disease, both cardiac and peripheral, and nephropathy; and 2) microvascular complications leading to retinopathy and neuropathies (Eckel, Grundy and Zimmet, 2005).

It is challenging, if not impossible, to clearly differentiate the impacts of diabetes from the impacts of the complications, because in many ways the complications are extensions of the disease. For example, rates of hypertension are higher in people with diabetes as a direct consequence of the disease. Sustained hypertension in the large arteries can lead to cardiac atherosclerosis and hence cardiac disease. Hypertension can lead to increased inflammation in peripheral arteries, plaque deposition and hence peripheral vascular disease (Inzucchi *et al.*, 2012). Increased blood pressure through the kidneys can lead to damage of the vascular bed that can significantly impair kidney function. Diabetes is the most common reason for developing end-stage kidney disease (DUK, 2012a).

Sustained hypertension in arterioles and capillary beds can lead to microvascular complications. Epithelial cell damage and inflammation within the capillary bed of the retina makes people with diabetes far more likely to develop glaucoma, cataracts and retinal degeneration than the population without diabetes (Tooke, 1995; DUK, 2010). Similar processes in Aβ and Að neurones affect afferent sensory information. Clinical signs of neuropathy develop in longer neurones, thus affecting the feet and lower extremities more often than the upper limbs (Waldman, 2000). Loss of the protective nociceptive information from the feet can expose people to tissue damage without conscious experience (Shah and Mueller, 2012). The reduced vascularity impairs healing often resulting in ulceration and potential need for amputation (Holt and Hanley, 2012a).

Reviews of the impact of diabetes highlight that improved treatment has reduced mortality as a direct result of the disease, but improved survival has increased the time available for potential complications to develop, hence overall morbidity due to diabetes has increased (Alberti and Zimmet, 2013). This is reflected in the ranking of diabetes, amongst worldwide causes for

disability, rising over the past 20 years (Murray *et al.*, 2012). As well as the difficulty of separating impacts from complications of diabetes, noted in the previous section, reviews have also highlighted the difficulty of separating the person with diabetes from the social situation in which they live. Social deprivation, smoking, alcohol intake and life stress have all been associated with the development of cardiovascular disease, depression and anxiety, and stress related disorders (Chapman, Tuckett and Song, 2008; Chrousos, 2009; Yoon, Kwok and Magkidis, 2012; Steno Diabetes Center/UCL, 2016).

### *1.2 Painful diabetic neuropathy*

Diabetic peripheral neuropathy, leading to sensory loss, is a common feature of diabetes affecting up to 50% of people (Lavery, Armstrong and Boulton, 2004; Boulton *et al.*, 2005). A proportion of people with neuropathy progress to experience pain due to neuropathy, termed painful diabetic neuropathy (PDN).

#### *1.2.1 Pathological process*

PDN is a significant complication of DM and is caused by a combination of processes which occur in the peripheral sensory nerves, at the dorsal horn of the spinal cord, and at higher cortical centres.

In the peripheral nerves, prolonged hyperglycaemia leads to the generation of reactive oxygen species (free radicals) and accumulation of advanced glycated end-products. Advanced glycated end-products are implicated in reducing the capacity of capillary membranes to vasodilate, and in the production and release of pro-inflammatory cytokines (Interleukines-1 and 6, Tumour Necrosis Factor-α) and nerve growth factors (Insulin-like growth factor and platelet-derived growth factor). The consequences of these multiple mechanisms are microvascular ischaemia, disruption to the mitochondrial energy supply for epithelial cells and damage to epithelial capillary linings (Tesfaye *et al.*, 2010; Shakher and Stevens, 2011).

These processes, initiated by hyperglycaemia, are specific to diabetes, but similar changes in peripheral nerves have been shown to contribute to neuropathic pain symptoms following chemotherapy (Wolf *et al.*, 2008), radiotherapy (Johansson, Svensson and Denekamp, 2000), excess alcohol consumption (Chopra and Tiwari, 2012) and anti-retroviral treatments for human immunodeficiency virus/acquired immunodeficiency syndrome (Schütz and Robinson-Papp, 2013).

The pathophysiological changes described above lead to structural epithelial cell damage, myelin sheath breakdown in Aδ-fibres and increased insertion of ion channels into the axolemma. An increased population of ion channels allows the axon to initiate ectopic (spontaneous) production of action potentials along afferent c- and Aδ-fibres, into the dorsal horn of the spinal

cord, hence increasing nociception (Woolf and Mannion, 1999; Baron, 2006). Charles Sherrington, who first described c-fibres, defined nociception as neural activity in response to the presence of noxious stimuli acting on receptors in peripheral tissues. The noxious stimuli, extremes of temperature, inflammatory mediators or mechanical force, would damage tissues if they continued to act (Woolf and Ma, 2007). It is important to be clear at this point that nociception is not the same as pain. These multiple processes contribute to peripheral sensitisation (Butler, 2000; O'Leary *et al.*, 2016).

At the dorsal horn of the spinal cord, persistent high levels of afferent nociception lead to a cascade of events termed central sensitisation. These events include: increased AMPA (alpha-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate) receptor activity; activation of NMDA (N-methyl-D-aspartic acid) receptors, which have slower kinetics so allowing more sodium ions to pass across the neuronal membrane; phenotypic changes in the neural cells to increase the production of AMPA receptors; and altered activity of glial cells (astrocytes). This cascade of activity leads to both reduced removal of excitatory neurotransmitters, and increased release of pro-inflammatory neurotransmitters into the local dorsal horn synapses and systemically (Latremoliere and Woolf, 2009; Allen and Barres, 2009).

As well as an increased excitatory drive, there is loss of inhibitory control from local interneurons and descending inhibitory control systems originating in higher cortical centres (Millan, 2002). The imbalance between excitation and inhibition creates an amplification of the transmission of action potentials from peripheral sensory neurones to ascending second order neurones. These multiple processes contribute to central sensitisation (Latremoliere and Woolf, 2009) and underpin the clinical presentations of allodynia (pain as a result of innocuous stimuli) and spontaneous pain that are particularly common, with neuropathic pain states.

Similar processes of increased neuronal excitation and reduced inhibition at higher cortical centres are thought to lead to the conscious experience of pain (Tracey & Mantyh 2007; Tracey & Bushnell 2009; Moseley & Vlaeyen 2015), although the exact processes leading to conscious perception are far from being fully elucidated (Thacker, 2015).

This story is one that builds from physics of molecular interaction, through biochemistry to biology and finally to the person. The person experiences a perception of pain and will interact with their social world in a variety of ways because of that perception, equally their social world has an effect on their perception of threat and pain (Engel, 1978).

*1.2.2 PDN presentation and diagnosis*

The multiple physiological processes lead to the development of burning pain in a 'glove and stocking' distribution that is usually constant, daily and moderate to severe intensity (Gore *et*

*al.*, 2006; Hoffman *et al.*, 2010; Koroschetz *et al.*, 2011). The pain is often not related to physical activity but spontaneous and unpredictable; it is often worse at night leading to disturbed and inadequate sleep (Zelman, Brandenburg and Gore, 2006). PDN is associated with significant impact on physical function and mobility (Bair *et al.*, 2010) as well as poor mood state and quality of life, over and above the impact of diabetes alone (Zelman *et al.*, 2005).

Clinicians need to consider differential diagnoses including neuropathy related to alcohol, vitamin B12 deficiency, neurotoxic medications (chemotherapies and anti-retroviral medications) or other musculoskeletal (nerve root pain) and vascular causes for pain (Doupis *et al.*, 2009; Hartemann *et al.*, 2011). Clinical examination considers the function of small diameter (temperature and light touch) and large diameter (10g monofilament test and 128Hz tuning fork) nerve fibers. Large diameter nerve function and nerve conduction studies can be normal in people with PDN (Hartemann *et al.*, 2011).

*1.2.3 PDN prevalence*

PDN affects 16-23% of people with DM (Daousi *et al.*, 2004; Veves, Backonja and Malik, 2008; Hartemann *et al.*, 2011), that is, approximately 600,000 people in the UK. The prevalence is higher for people with T2DM (18%), than T1DM (6%) (Hartemann *et al.*, 2011). There is concern, particularly for the population who have T2DM, that increasing prevalence of DM and earlier development of prediabetes states, leads to longer periods of time for the person to develop microvascular complications because of hyperglycemic physiological consequences (Alberti and Zimmet, 2013).

*1.2.4 The impact of PDN*

*1.2.4.1 Severity of pain*

In cross sectional studies 15-20% of participants rated their pain as ‘mild’, 47-57% as ‘moderate’ and 25-33% as ‘severe’ (Davies *et al.*, 2006; Tölle, Xu and Sadosky, 2006). A survey of patients with PDN (n=255) found ‘average pain’ was rated as mean 5.0 (SD2.5)/10, and ‘worst pain’ rated as mean 5.6 (SD2.6)/10 (Gore *et al.*, 2006). A further cross-sectional study found 12.5% of those with PDN had never disclosed their symptoms to a clinician, and 39.3% had never received treatment for their symptoms (Daousi *et al.*, 2004). This suggests that PDN may have been a hidden problem when this study was conducted. A recent audit of UK pain clinic data found neuropathic pain under-represented, which suggests this may still be the case (BPS, 2012).

*1.2.4.2 Impact on mood*

Diabetes is associated with increased prevalence of depression and anxiety when compared to people without diabetes (Collins, Corcoran and Perry, 2009), please see section 1.1.6 above. Persistent pain of all causes is associated with higher prevalence of depression (Campbell, Clauw

and Keefe, 2003) and anxiety (McCracken *et al.*, 1999). It is perhaps not surprising that the coexistence of both DM and pain is positively associated with depression and anxiety.

Data for rates of anxiety and depression from a PDN study (Gore *et al.*, 2006) are presented in Table 1, in comparison to data from a postal survey establishing the normative data for the Hospital Anxiety and Depression Scale (HADS) outcome measure (Breeman *et al.*, 2015). Both mood states are notably worse in the PDN cohort.

Table 1 - Comparative Hospital Anxiety and Depression Scale data for PDN and healthy controls

| ***HADS category*** | **% Anxiety** | | **% Depression** | |
|---|---|---|---|---|
| | **PDN[1]** *n=265* | **HC[2]** *n=6189* | **PDN[1]** | **HC[2]** |
| ***Normal*** | 38.0 | 66.7 | 48.2 | 83.7 |
| ***Mild*** | 25.1 | 17.0 | 22.4 | 9.5 |
| ***Moderate/Severe*** | 35.3 | 16.1 | 28.2 | 6.9 |

*HADS – Hospital Anxiety and Depression Scale. HC – Healthy controls. PDN – Painful diabetic neuropathy. [1] Gore et al. (2006), [2] Breeman et al. (2015)*

*1.2.4.3 Impact on function*

Studies have quantified the impact of PDN on function using a range of outcome measures. The EuroQol (EQ5D) measure of health status asks five questions, including a pain rating question, to calculate a life utility score between 0.0 (equates to death) and 1.0 (equates to perfect life utility). Study participants rated their life utility as 0.59-0.63 (mild pain), 0.43-0.52 (moderate pain) and 0.2-0.25 (severe pain) (Currie *et al.*, 2006; Tölle, Xu and Sadosky, 2006).

Other studies have used the Brief Pain Inventory (BPI) as an indicator of function; scores toward 10, represent a greater interference of pain on function. The results of three studies are detailed in Table 2. Two studies are presented as representative of PDN research (Galer, Gianas and Jensen, 2000; Hoffman *et al.*, 2010), and a third comparison study that used the BPI with people experiencing low back pain (LBP) (Song *et al.*, 2016). All aspects of function measured by the BPI are notably worse with PDN than LBP. The domains for activity, walking and sleep quality have been consistently rated as impaired by the experience of PDN.

Table 2 - PDN impact on function

| ***BPI subscales*** | **PDN** | | **LBP** |
|---|---|---|---|
| | Galer, Ginas and Jensen (2000) n=105<br>Mean (SD) | Hoffman *et al.* (2010) n=400<br>Mean (SD) | Song *et al.* (2016) n=271<br>Mean (SD) |
| ***General activity*** | 4.33 (3.15) | 5.5 (2.5) | 2.03 (2.34) |
| ***Mood*** | 4.04 (3.02) | 5.5 (2.7) | 3.25 (2.66) |
| ***Walking ability*** | 4.63 (3.13) | 5.6 (2.7) | 3.32 (2.61) |
| ***Normal work*** | 4.70 (3.21) | 5.1 (2.8) | 3.50 (2.77) |
| ***Relationships*** | 3.13 (2.90) | 4.3 (2.8) | 1.76 (2.26) |
| ***Sleep*** | 5.38 (3.25) | 5.5 (2.9) | 2.80 (2.88) |
| ***Enjoyment of life*** | 5.00 (2.89) | 5.1 (2.8) | 2.69 (2.66) |
| *BPI – Brief pain inventory, PDN – Painful diabetic neuropathy, LBP – Low back pain* | | | |

The SF36 outcome measure can be presented as physical and mental composite summary scores. Scores nearer to 100 represent higher levels of function. A study comparing people with PDN (n=290) to matched cases with diabetes but without PDN (n=1,037) found no difference in the mental composite scores (50.51 (PDN) to 50.98 (DM), p=0.24). People with PDN however, scored significantly lower on the physical composite scale (41.58 to 46.07, p=0.0001) (DiBonaventura, Cappelleri and Joshi, 2011).

*1.2.4.4 Impact on sleep*

Studies investigating sleep found PDN was associated with disturbed sleep, as measured by the Sleep Problems Index, and with reduced sleep quantity and adequacy. The impact on sleep was significantly greater than the comparison data for both the US population generally (all $p<0.001$), and for a sample with chronic pain (all $p<0.001$) (Zelman, Brandenburg and Gore, 2006). These data highlight the specific impact neuropathic pain appears to have on measures of sleep. A recent study examined the associations between sleep quality (Medical Outcome Study Scale (MOS)) and mood (HADS). There was a positive association between sleep disturbance and pain ($r$=0.40, $p<0.001$) and between sleep disturbance and depression ($r$=0.30, $p<0.001$) (Hughes *et al.*, 2016).

*1.2.4.5 Impact on work*

People with PDN are no more likely to be off work (absenteeism) than people with diabetes alone (4.74% to 3.49%, p=0.28), but are more likely to self-evaluate being at work, but unable to fully complete their job role (presenteeism) (17.84% to 13.52%, p=0.022), and to rate themselves

as having overall work impairment (19.77% to 13.75%, p=0.028) (DiBonaventura, Cappelleri and Joshi, 2011).

*1.2.4.6 Impact on healthcare systems*

A number of studies have investigated healthcare costs associated with PDN. Data have demonstrated that routine and emergency medical appointments, and the cost of medication increase in line with pain symptom severity (Alleman *et al.*, 2015). Using data from Tölle *et al.* (2006) and converting to 2013 costs, Alleman *et al.* (2015) demonstrated yearly healthcare costs rising from €2,375 (mild pain) to €3,795 (severe pain).

Using 2006-2008 data from Insurance databases in the USA, DiBonaventura *et al.* (2011) calculated the total direct (hospital/primary care visits) and indirect costs (lost income from absenteeism and presenteeism) associated with PDN to be $28,428 across two years, ($17,440 diabetic control cases, $15,981 healthy control cases).

*1.3 Current management for PDN*

The most logical strategy for preventing PDN would be to reduce neuropathy from developing in the first place. Research investigating enhanced glucose control for prevention and treatment of neuropathy have been systematically studied (Callaghan *et al.*, 2012). Seven studies investigated T1DM. The homogeneity of two high-quality studies allowed the conduct of meta-analysis (n=1,228), the results of which showed the annualised risk difference to be -1.84% (CI -1.11 to -2.56) for developing clinical neuropathy, in participants using enhanced glucose control approaches. Eight studies focussed on T2DM, four studies were sufficiently homogeneous to allow meta-analysis (n=6,669), demonstrating a risk difference of -0.58% (CI 0.01 to -1.17), indicating no significant difference between enhanced glucose control and usual care. The authors recorded secondary outcome data of adverse events rates. Participants in the enhanced glucose control intervention arms experienced higher rates of hypoglycaemic episodes (62 episodes requiring assistance per 100-patient years, compared with 19 in the control arms, p<0.001). The review concluded that enhanced control appears to protect against the development of PDN for T1DM more so than T2DM, but the increased risk of hypoglycaemia needs to be considered (Callaghan *et al.*, 2012).

When PDN has been diagnosed, a range of medication options are recommended (Bril *et al.*, 2011; NICE, 2010, 2013a; NHS BNSSG, 2012). In the UK, NICE guidance (NICE 2010) for PDN recommended Duloxetine as first-line therapy, or Amitriptyline if Duloxetine was contraindicated. Second-line therapy recommendations were to switch to Amitriptyline or combine with Pregabalin if Duloxetine was the first-line drug; or switch to, or combine with Pregabalin if Amitriptyline was the first-line drug. If suitable pain relief was not achieved with second-line

drugs, then referral to specialist units, and consideration of short-term Tramadol as a third-line drug was suggested. Stronger opiates such as morphine were not advised.

The American Academy of Neurology guidance differed slightly to that from NICE. Pregabalin was recommended with Level A evidence (established as effective in at least two Class 1 studies (high quality randomised controlled study design)) and Gabapentin, Duloxetine and Amitriptyline with Level B evidence (probably effective in at least one Class 1 study or two consistent Class 2 studies (moderate quality randomised controlled study design)) (Bril *et al.*, 2011).

For the UK reader, it is important to note the guidance for medication had evolved between NICE 2010 and NICE 2013 to become less certain and prescriptive (NICE, 2013a). This was partly due to economic reasons. The license for Pregabalin ended in 2014 thus allowing generic manufacture and so a reduced cost. In addition, Finnerup *et al.* (2015) in a comprehensive meta-analysis found the 'number needed to treat' (NNT) for the four main neuropathic pain medications ranged from 3.6 (Amitriptyline) to 7.7 (Pregabalin). Furthermore when data were examined by individual case, rather than by population average, patients were found to either 'respond' or 'not respond' to a class of medication (Moore, Derry and Eccleston, 2013). Response to medication does not follow a typical bell-shaped Gaussian distribution (Moore, Derry and Eccleston, 2013).

The current guidance from NICE (NICE 2013) suggests there is no preferable first line therapy, rather clinicians select from Amitriptyline, Duloxetine, Pregabalin and Gabapentin depending on contra-indications, effectiveness on subsequent patient review and patient reported side-effects. There are a sizeable proportion of patients with PDN who do not experience adequate management of pain symptoms, or the consequent impacts, with these drugs (Moore, Derry and Eccleston, 2013; Finnerup *et al.*, 2015).

If successful management of pain symptoms, and its impacts, is not achieved with the recommended drugs, NICE recommend referral on to specialist pain services.

### *1.3.1 Current research programmes for PDN treatment*

There are research programmes currently underway, investigating novel approaches to PDN management. Spinal cord stimulation has been explored in a multi-centre randomised trial (de Vos *et al.*, 2014). Sixty patients with PDN were randomised 2:1 into the stimulation arm or the control arm. These arms were similar for social and clinical variables at baseline but potential participants with depression were excluded. Studies have found half the population (52%) with PDN were rated depressed to some degree, and 28% as moderate to severely depressed (Gore *et al.*, 2006). This exclusion criterion raises the possibility that the study participants do not

accurately represent the population with PDN. At six-month follow up there had been no significant change in control arm pain scores (Visual Analogue Scale (VAS) mean 67(SD18) to 67(SD21), non-significant) but a significant decrease in the intervention arm (mean 73(SD16) to 31(SD28), $p<0.001$). In the intervention arm, 25/40 (60%) participants experienced >50% pain reduction.

A randomised, placebo controlled study investigated the efficacy of inhaled cannabis for PDN (Wallace *et al.*, 2015). Using tetrahydrocannabinol (THC) of different strengths (1%, 4% and 7%) delivered by aerosol, the study found reductions in spontaneous pain of 63.8% (SD37.0) (1%, non-significant), 64.8% (SD36.0) (4%, $p<0.10$) and 69.0% (SD32.0) (7%, $p<0.05$), when compared to placebo inhalant (52.8% (SD40.0). The study was small (n=16) and participants were randomised between THC and placebo arms. The study had a short follow up, measuring effects to three hours from first dose. The participants who were delivered the 7% THC dose performed least well on three neurocognitive tasks.

Two studies investigating Botulinum toxin-A (BTX-A) efficacy for PDN were included in a recent meta-analysis (Lakhan, Velasco and Tepper, 2015). Both studies injected BTX-A into 12 sites in a grid pattern on the dorsum of the participants' feet. The toxin is absorbed by the afferent neurones and transported to the synapse in the dorsal horn. BTX-A inhibits the release of various neurotransmitters at the dorsal horn synapse, notably the excitatory amino acid glutamate. The two studies were double blinded, with one a crossover design (Yuan, Sheu and Yu, 2009) and the second a placebo-controlled design (Ghasemi, Ansari and Basiri, 2014). Participant numbers were small (n=18 and n=20). The meta-analysis showed that BTX-A resulted in reduced pain on a VAS by -1.96 points (CI -3.09 to -0.84, $p<0.001$) at the four-week follow up. There was one adverse event reported of an injection site infection.

A systematic review of psychological therapies for neuropathic pain in adults, found nine studies listed in trials registers as currently underway but results were not yet available (Eccleston, Hearn and Williams, 2015).

### *1.4 Current concepts and models for pain – A short history*

This thesis will explore the lived experience of physical pain in people with PDN. Pain is a complex experience that goes to the heart of our understandings of perception and consciousness. There have been key stages of development to our present knowledge of pain mechanisms that will be outlined. The description of these developments will allow an appreciation for the state of the art in pain research, and also highlight the interdependence between clinical and basic science research.

The word *pain* can be traced to the French *peine,* and further to the Latin *poena*, which translates as *penalty* or *punishment.* Prior to the Middle ages, little was known about the physiology of pain, but the experience of pain was considered as a punishment from God, for sins committed (Lewis, 1940).

Introductions to pain often start with the French philosopher and mathematician René Descartes (1596-1650). In *Treatise of Man* (1664), Descartes described a pathway between peripheral stimuli to the body and the pineal gland in the brain, where he proposed all conscious thought and experience resided (see Figure 3 below). The division between body and brain, Cartesian Dualism, allowed scientists to research these pathways in greater detail while allowing the Church to retain ownership of the soul (Sullivan, 2008). Although 350 years old, Dualism can still be seen in both academic and popular science writing about pain. It is common to see diagrams labelled with pain receptors, pain nerve fibres, and pain centres in the brain. These diagrams have the implication that pain is external to the corporeal body, sensed by pain receptors and then transmitted into the brain along pain-specific nerve pathways.

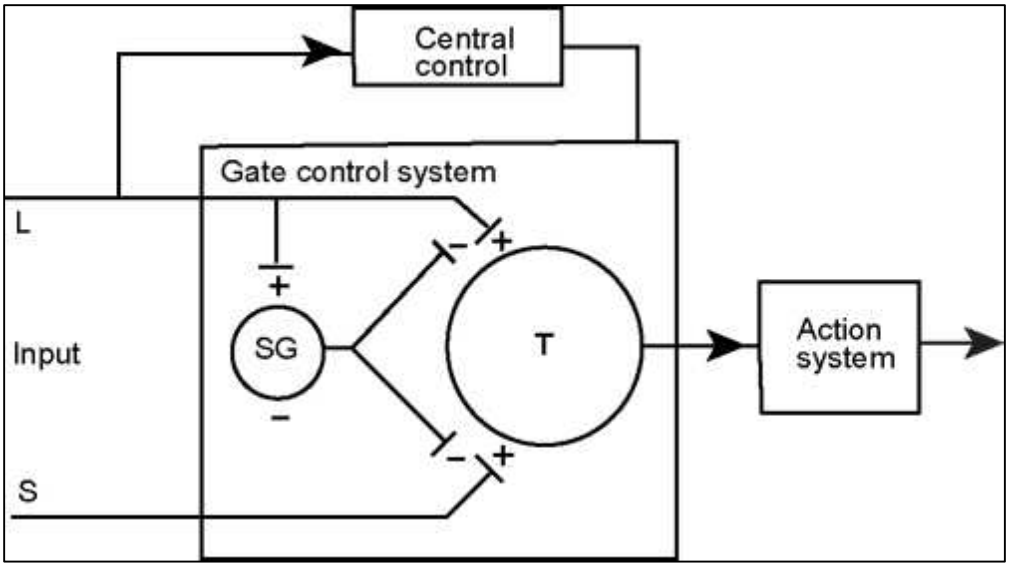
Figure 3 - Rene Descartes model of pain - Treatise of Man (1664) *(copyright permission not required)*.

A significant development came in 1965 with Melzack and Wall publishing the Gate Control Theory of Pain (Melzack, 1999). The Gate Control Theory (Figure 4) demonstrated how descending neural messages from higher limbic brain centres (L), were able to excite spinal gate neurones (SG). An increased discharge from SG neurones, would lead to inhibition of the incoming sensory (S) information at the synapses in the spinal cord. This model highlighted that the experience of pain was not solely dependent on peripheral stimuli, but that higher centres of the brain had the capacity to attenuate the peripheral stimuli, both in an inhibitory or facilitatory manner. Wall argued that this explained many of the inconsistencies between pain and injury observed in clinical practice (Wall, 1999).

Although the Gate Control Theory was significant in moving pain science forward by giving the brain more than a role as passive *receiver* of pain, Melzack was clear the theory was not

sufficient to explain all clinical pain presentations (Melzack, 1990, 1999, 2005). He highlighted that this model did not account for the pain people experienced after a stroke or the phantom pain that could exist even in congenital missing limbs.

Figure 4 - Melzack and Wall, Gate Control Theory 1965 (Melzack 1999) *(reproduced with permission)*



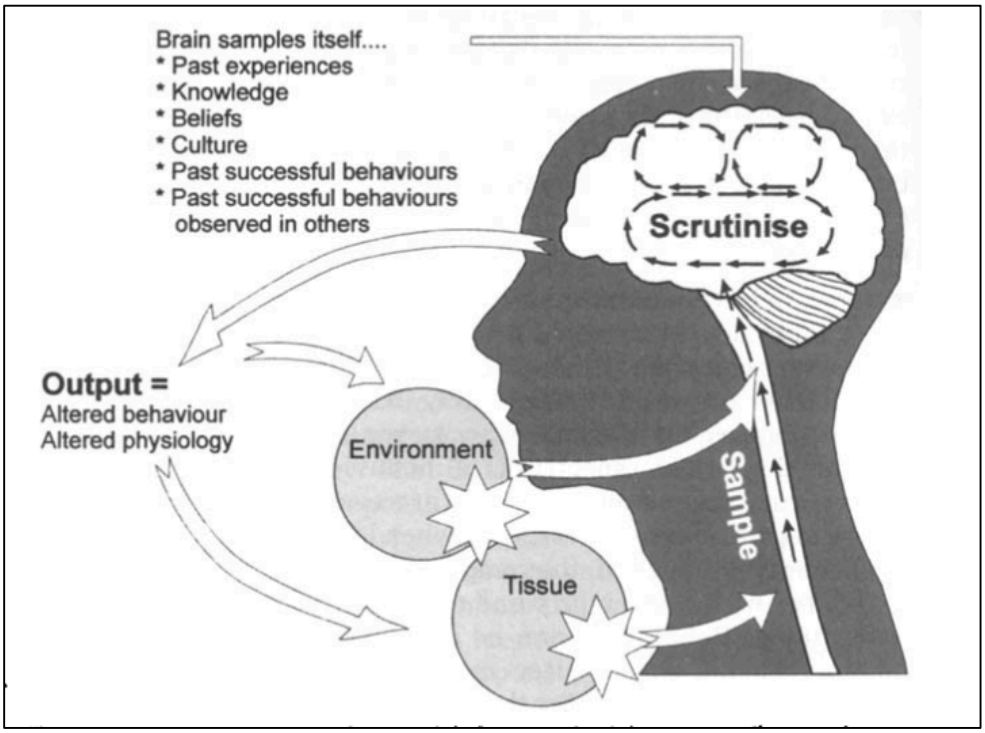

L – Limbic system, S – sensory system, SG – Spinal gate neurone, T – Thalamic relay neurone, + - excitation, - inhibition.

*1.4.1 The Mature Organism Model*

The next phase in the development of comprehensive models for pain came from Louis Gifford, with the publication of the Mature Organism Model (MOM) (Gifford, 1998a) and from Melzack, with the publication of the Pain Neuromatrix model (Melzack, 2001).

Gifford's MOM (see Figure 5 below) contains an input arm, where the organism (person) is continually sampling from itself (tissues) and from the environment. The sampled information is then scrutinised by the brain and given weight dependent on that person's life experience - how dangerous is this situation? Is there tissue damage present? What strategies have/have not worked in the past? This central decision-making process leads to a variety of outputs that include pain experience, motor system, cognitive system, stress system and behavioural changes that are deemed most appropriate for survival and the restoration of homeostasis. Gifford described this as a 'Mature' organism model, because the persons' life experiences sculpt the scrutinising and weighting process toward, or away from, a range of behaviours. The selected behaviours give feedback into the process of scrutiny. In clinical practice this means the person's pain experience and other system outputs cannot be divorced from the narrative of their life.

Figure 5 - Mature Organism Model (Gifford 1998) *(reproduced with permission)*.

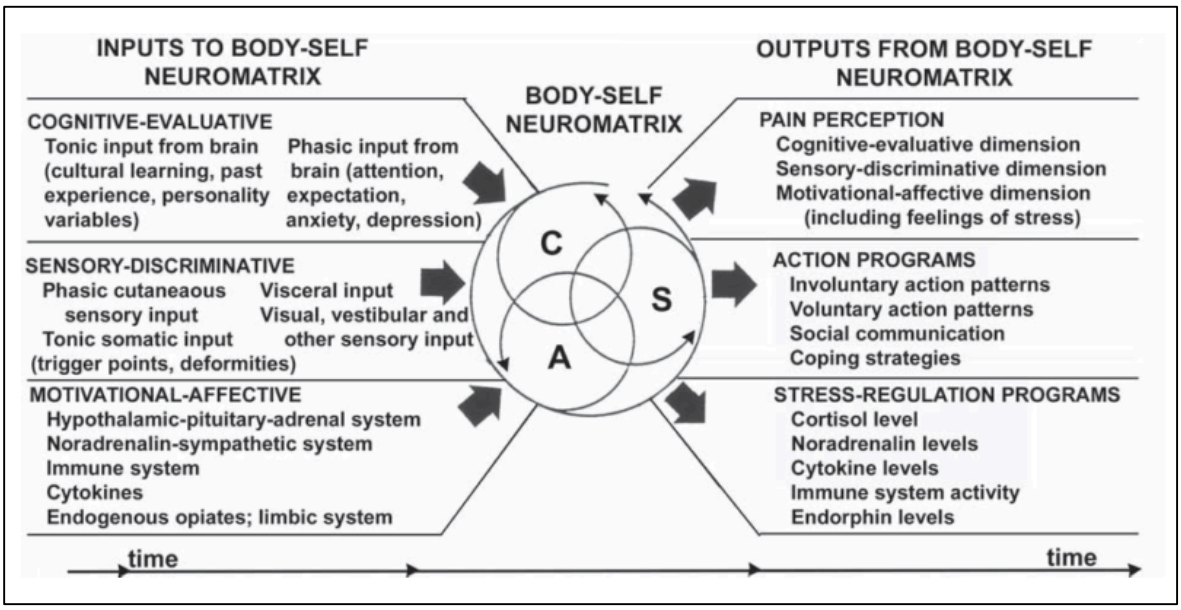



*1.4.2 The Neuromatrix Theory*

Melzack published the Neuromatrix theory at a similar time to Gifford's MOM (Melzack, 1999). The Neuromatrix (see Figure 6 below) includes input from the body (cutaneous, visual, and vestibular inputs), other physiological systems (immune system and stress system) and from the person's life (culture, past experiences). This information is processed in the central part of the model, and from this processing emerges a range of outputs. These outputs include the experience of pain with its sensory, cognitive and affective components. These outputs include motor action programmes (behaviours) and adaptations within the immune and stress regulatory systems.

The Neuromatrix is abstract and conceptual; Melzack did not suggest precise anatomical locations. The Neuromatrix should not be conflated with an anatomically located Pain Matrix (Tracey and Johns, 2010). While regions of the brain have been implicated in the processing of threat and pain (Tracey and Mantyh, 2007; Tracey and Bushnell, 2009), these same regions are also implicated in the processing of pleasure (Leknes and Tracey, 2008).

Figure 6 - The Neuromatrix Theory (Melzack 2001) *(reproduced with permission)*




A – affective processing, C – cognitive processing, S – sensory processing

Although with different textual descriptions and schematic diagrams, the MOM and the Neuromatrix theory display similar ideas about the complexity of pain. An important distinction to previous models is they place pain as an output, rather an input. Said in another way, pain is created by the synchronous activity of multiple immune and neural systems, and is experienced by the person (Thacker and Moseley, 2012). These models both identify that pain perception does not occur in isolation, but as part of a response that includes other systems. This symphony of responses is dependent on the situational context, the salience and meaning the person subconsciously gives to that situation (Iannetti and Mouraux, 2010; Moseley and Flor, 2012). Further, these responses are sculpted by the success and failures that we all experience through life.

The recursive nature of these models can explain why some output responses may become inappropriate for the context of the person in pain. These responses may have been adaptive in the short term around the time of an injury, but have become maladaptive in the long term when that tissue injury has healed (Moseley, 2007; Chapman, Tuckett and Song, 2008). These models and theories add support to the biopsychosocial approach to persistent pain (Engel, 1978).

*1.5 Pain management programmes*

Integrated biopsychosocial models such as the MOM and Neuromatrix are helpful when treatments aimed at pain reduction are unsuccessful. Pain management programmes (PMPs) aim to help individuals live well with pain and typically involve multidisciplinary clinical teams of medics, psychologists, physiotherapists, occupational therapists and nurses (BPS, 2013). The

specific team mix varies dependent on the PMP provider. Despite their name, programmes tend to focus on quality of life, rather pain reduction (Moseley and Butler, 2015).

A recent systematic review of multidisciplinary PMPs for LBP included 41 studies (n=6,858 participants) (Kamper *et al.*, 2015). All included studies compared multidisciplinary PMPs against non-multidisciplinary approaches. The authors concluded PMPs reduce pain by a standardised mean difference (SMD) of -0.21 (CI -0.04 to -0.37, p=0.01), this was calculated as equivalent to a 0.5-point reduction on a 10-point scale for pain. The PMPs also reduced disability by a SMD -0.23 (CI -0.06 to -0.40, 0=0.007). They found evidence that attending a PMP increased the likelihood of being in work at one year by odds ratio 1.87 (CI 1.39 to 2.53, p<0.001).

The British Pain Society (BPS, 2013) recommend multidisciplinary teams of clinicians are the *"treatment of choice for people who experience persistent pain that is adversely affecting their quality of life and where there is significant impact on physical, psychological and social function"* (Executive summary 1.2-1.2). This recommendation was based on evidence from high quality randomised trials and systematic reviews of pain management research, including meta-analysis of outcome data, graded 1++ in the Scottish Intercollegiate Guideline Network level of evidence.

The British Pain Society recommends that the content of the PMP should include education on pain mechanisms, general health and self-management strategies, guided practice of exercise and challenge to unhelpful beliefs, behaviours and habits that may contribute to disability (BPS, 2013). The key recommended interventions are physical rehabilitation and psychologically focussed treatment - these will be examined in more detail in the following sections (section 1.5.1 and 1.5.2). Other topics within PMPs can include sleep strategies, stress management strategies and communication skills training. The curriculum of PMPs are often based on the particular interests of clinicians involved in their inception and delivery (Ehde, Dillworth and Turner, 2014). The British Pain Society acknowledges that a variety of course content, intensity and delivery formats have been implemented and researched.

### *1.5.1 Physical activity in PMPs*

Central tenets of PMPs are strategies of graded physical activity or exercise. The physical approach aims to promote cardiovascular fitness and functional capacity that will allow a person to achieve goals and valued life activity. This may be a graded increase in day-to-day activity, or a structured exercise program. Exercise may include hydrotherapy, Tai Chi-type movement, cardiovascular exercise or resistance strength training. There is uncertainty about what type of exercise is optimal for pain. A recent systematic review of muscle stabilisation exercises for the management of LBP found this specific approach to be effective for reducing pain (VAS) when compared to alternative, non-physical exercise treatments (pain reduction (0-100 scale) mean -

6.39 (CI -10.14 to -2.65)). When stabilisation exercises were compared with other exercise approaches, the reduction in pain was non-significant (pain reduction mean -3.06 (CI -6.74 to 0.63)) (Smith, Littlewood and May, 2014). Although statistically significant the absolute reduction in pain did not approach the minimal clinically important difference for pain (reduction of 24-40 on 0-100 scale) (Smith, Littlewood and May, 2014).

A Cochrane overview of physical activity and exercise for chronic pain of all causes was recently published (Geneen *et al.*, 2017). Twenty-one reviews (381 studies) were pooled covering a range of pathologies associated with persistent pain, which included rheumatoid arthritis, osteoarthritis and spinal disorders amongst others. PDN was not a specific pathology but neuropathic pain was represented by the inclusion of fibromyalgia syndrome (FMS), post-polio syndrome and spinal cord injury. The authors included any form of physical exercise, and specified reported pain severity as the primary outcome with physical and psychological function and quality of life as secondary outcomes. The included primary studies were often small, with 223/264 (84%) having <50 participants per study arm. It has been suggested that studies should aim to recruit more than 50 participants (100 in total in a 2-arm study) to minimise bias from regression to the mean (Moore *et al.*, 2010). Most studies also lacked long-term follow up beyond six-months.

Most of the included reviews demonstrated beneficial effects of exercise on pain severity, but these results have inconsistencies between the exercise interventions, participant pathology and follow-up time points. Other than transient soreness after exercise, no reviews reported worsening of pain following exercise protocols. There were more consistent improvements in measures of physical function and health-related quality of life. Fourteen of the 21 reviews found statistically significant improvements in physical function and these had small to moderate effect sizes (Geneen *et al.*, 2017). The conclusion was that physical exercise appears to benefit function and quality of life for those with persistent pain, and may improve pain severity.

### *1.5.2 Psychological treatment in PMPs*

An equally important central tenet of PMPs is strategies to help people deal with the psychological distress that can occur alongside on-going pain. This distress can include stress, anger, guilt, depression, anxiety or a combination of the above. Distress can manifest in maladaptive behaviours, such as avoidance and social withdrawal, which may further reduce physical fitness, mood state and social contact (Vlaeyen and Linton, 2000). Psychological coping strategies aim to help people develop psychological and behavioural techniques to mitigate these manifestations of distress, and so improve their pain experience and overall quality of life (BPS, 2013). Clinical practice and research are most often based on principles of Cognitive Behavioural Therapy (CBT) and Acceptance and Commitment Therapy (ACT).

The goals of CBT have been described as "*to reduce pain and psychological distress and to improve physical and role function by helping individuals decrease maladaptive behaviours, increase adaptive behaviours, identify and correct maladaptive thoughts and beliefs, and increase self-efficacy for pain management*" (Ehde, Dillworth and Turner, 2014). A recent Cochrane review for psychological therapies for chronic pain found 42 eligible studies (Williams, Eccleston and Morley, 2012). These randomised trials were with adults and had used recognised psychological frameworks or models in their intervention arm. The review found CBT had a small effect on pain reduction when compared to treatment-as-usual at the end of the treatment course (SMD) -0.21 (CI -0.37 to -0.05, p<0.05)). This effect was not significant at longer-term follow up. The authors found CBT had a beneficial effect on mood at the end of treatment (SMD -0.38 (CI -0.57 to -0.18, p<0.01)) though this effect became non-significant at long term follow up (SMD -0.26 (CI -0.51 to 0.00, p=0.05)). Lastly, they found CBT reduced disability (SMD -0.19 (CI -0.33 to -0.05, p<0.01), and although this effect was reduced at longer term follow up it remained significant (SMD -0.15 (CI -0.28 to -0.02, p<0.05). There was no effect when active treatment (for example, exercise programme or pain related education) was the comparator arm.

Williams, Eccleston and Morley (2012) concluded that CBT demonstrated small benefits on pain, mood and disability immediately post-treatment when compared against treatment as usual. They suggested future research should not examine outcome changes at the group level, but focus on trying to establish what features of CBT are effective for which patient groups, and on which outcome domains.

The other psychological approaches used in PMPs are ACT which has developed from CBT, and Mindfulness-based stress reduction (MBSR) (Morley and Williams, 2015). ACT focuses on accepting pain and related cognitions, rather than trying to challenge and reappraise these, as with CBT (Veehof *et al.*, 2011; McCracken and Vowles, 2014). ACT aims to help people use their resources (time, energy, motivation) in living towards important life values, and to reduce behaviours that try to change the unchangeable. Values differ from goals in being unobtainable yet central to the person's core sense of self (for example, being a perfect parent is unobtainable) (McCracken and Yang, 2006). MBSR has origins in Buddhist teachings. Similar to ACT, MBSR emphasises being present with pain, rather than fighting the experience.

A systematic review included 19 eligible studies investigating ACT and MBSR in the management of chronic pain (Veehof *et al.*, 2011). Ten controlled studies (randomised and non-randomised methods) were included in meta-analyses. The interventions were compared against waitlist, treatment as usual or educational interventions. For pain severity, the results showed a moderate effect size of SMD 0.37 (CI 0.20 to 0.53, p<0.01) favouring the intervention arms. The effect on overall quality of life (n=6 studies) was found to have SMD 0.41 (CI 0.16 to 0.65, p<0.01)

favouring the intervention arms. Key researchers in the field suggest the literature relating to CBT and ACT approaches to pain are reaching a level of maturity (McCracken and Thompson, 2011). Rather than future studies comparing active treatment to placebo or treatment as usual, to investigate whether the individual approach is effective, studies should focus on elucidating which approach works for whom (Vlaeyen and Morley, 2015).

The Cochrane review (Williams, Eccleston and Morley, 2012) described above, included pain of many causes and pathologies. This breadth of presentations and pathologies may cause meaningful changes within some participant sub-groups to be obscured. Authors have suggested that considering all chronic pain as homogenous is an important error and that efforts should focus on understanding how different people, or different underlying pathologies may react differently to the same intervention (Turk and Okifuji, 2003; Turk, 2005). This would allow more patient-specific delivery of treatments.

*1.5.3 Should people with neuropathic pain be considered a distinct subgroup?*

It could be appropriate to consider neuropathic pain as a distinct subgroup for a number of reasons. Neuropathic pain has associations with defined disease processes, for example, multiple sclerosis (MS), alcoholic neuropathy and PDN; or, as a side-effect of specific treatments, for example, radiotherapy-induced neuropathy, chemotherapy-induced neuropathy and neuropathy due to anti-retroviral treatments for human immunodeficiency virus. This specificity is in contrast to non-specific diagnostic labels used for LBP, whiplash associated disorder and FMS (Daniel and Van der Merwe, 2006). Neuropathic pain has different symptom profiles (unpredictable, burning quality, often worse at night), than either nociceptive pain mechanisms (predictable provocation, dull ache, lack of sleep disturbance) or central pain mechanisms (diffuse non-anatomical locations, pain disproportionate to nature and extent of tissue dysfunctions, strong association with maladaptive psychosocial factors) (Smart *et al.*, 2012a, 2012c, 2012b). The series of studies by Smart *et al.* (2012a, b and c) used Delphi survey techniques to reach consensus from clinical experts on the presenting patterns for these pain mechanisms. The authors were clear to highlight that patients do not present with pain purely from one mechanistic process, but they were on a continuum from mostly tissue based (very acute injury pain) to mostly central process based (post-stroke pain) (Smart *et al.*, 2010).

Differences have been demonstrated between patient presentations of neuropathic and nociceptive pain. A study compared the profile of people with mechanical LBP (n=57), considered a model of nociceptive pain, against post-herpetic neuralgia (PHN) as a model of neuropathic pain (n=49) (Daniel *et al.*, 2007). Logistic regression showed that having pain aggravated by touch and air movement were predictive of belonging to the PHN group. Allodynia (pain on light tough) was experienced by 32% of the PHN group but none of the LBP group. Pacing, a standard approach to

the management of LBP, had not been found useful by any respondents with PHN. The PHN group were significantly more likely to describe the cause of their pain as 'nerve damage', whereas the LBP group were more ambiguous in their answers, or stated they did not know the cause.

Martin *et al.* (2014) researched the issues of patient belief about pain. Using Q-methodology they explored how patients with neuropathic pain conceived of the causes and impacts of their pain and outlined three factors of shared subjective experience relevant to this thesis. Participants in factor 1 conceived neuropathic pain as due to nervous system dysfunction, stated that psychology had an impact on the experience and were open to psychologically directed treatments. Participants in factor 2 conceived neuropathic pain as due to nervous system dysfunction, rejected psychological factors as relevant to their pain experience and were neutral to psychologically directed treatments. Participants in factor 3 felt nerve damage was irreparable, reported psychological factors were relevant to their pain, but rejected psychologically directed treatments as relevant. People with PDN have a diagnostic label for the cause of their pain, and it is of interest to explore openness (or lack of) to psychological approaches.

It is accepted that neuropathic pain presents differently to musculoskeletal pain (Haanpää *et al.*, 2011). Despite this, previous Cochrane reviews of psychological therapy included pain of all causes, except headaches (Williams, Eccleston and Morley, 2012). Eccleston, Hearn and Williams, (2015) therefore conducted a systematic review specifically investigating psychological therapy for neuropathic pain conditions. Two studies were included in the review, each with a high degree of bias, resulting in no recommendations for treatment (Eccleston, Hearn and Williams, 2015).

The modest treatment effect sizes found across pain, mood and disability outcomes could be considered a reason to abandon psychological therapies for pain. Leading authors in the field suggest future research should measure how credible participants deem the intervention to be as well as their expectations of the intervention (Vlaeyen and Morley, 2015). The modest treatment effects observed might be partially due to some participants having a low expectation of the intervention and not considering it credible or related to the problems they experience.

There is evidence that neuropathic pain is different in its clinical presentation, particularly considering nocturnal pain and spontaneous flare. People with primary neuropathic pain are not frequently referred to PMPs (Daniel *et al.*, 2015) and the clinical experience of the researcher and others, suggests not all standard PMP strategies are appropriate for neuropathic pain problems. People with neuropathic pain hold a range of beliefs regarding pain and whether psychological state is relevant to the problems they experience (Martin, Daniel and Williams, 2014). This range of beliefs will affect whether psychological interventions are deemed credible and acceptable. It is therefore appropriate to explore these issues with people who experience PDN.

## *1.6 Purpose of the thesis*

### *1.6.1 Thesis rationale*

There are evidenced guidelines for the pharmacological management of neuropathic pain (NICE, 2010, 2013a) and PDN specifically (Bril *et al.*, 2011). These guidelines do not fully concur resulting in clinical uncertainty (Spallone, 2012). Previous research has shown that patients with PDN are frequently taking analgesia not recommended within these guidelines (over the counter anti-inflammatories), and even when they are taking recommended medication their ratings for satisfaction and effectiveness are low (Gore *et al.*, 2006).

Although PMPs have been shown to be clinically and cost effective for the management of musculoskeletal persistent pain (Gatchel and Okifuji, 2006; Williams, Eccleston and Morley, 2012), it is unclear whether the strategies contained within them are appropriate for the person with PDN or, if the person with PDN would be inclined to attend such a programme. Clinicians involved with PMPs identify that people with PDN are infrequently referred and strategies may not be appropriate to neuropathic pain (Daniel *et al.*, 2015). Beyond medication, physical exercise and psychological coping strategies, there are limited evidenced therapeutic options for persistent pain and associated impacts, so the strategies available need to be as tailored and specific as possible.

### *1.6.2 Thesis aims*

1) To conduct a systematic literature review of the evidence investigating physical activity and psychological coping strategies, in the management of PDN.
2) To explore peoples' experiences of living with and self-managing PDN, and their perspectives on physical activity and psychological coping strategies for PDN management.
3) To explore specialist clinicians' current strategies for management of PDN (as one form of diabetic complication), and their perspectives on physical activity and psychological coping strategies for PDN management.
4) To explore which impacts of PDN people prioritise for improved, or alternative, management strategies.

### *1.6.3 Thesis objectives*

1) To source and critically appraise the current research that investigates physical activity and psychological coping strategies in the management of PDN (Chapter 2).
2) To conduct semi-structured interviews with people who experience PDN finding out how PDN impacts on their lives and how they currently manage (Chapters 3 and 4).

3) To explore within those interviews the participant perspectives on physical activity and psychological coping strategies for the management of PDN (Chapters 3 and 4).
4) To explore using semi-structured interviews how clinicians currently view management strategies for PDN, and to explore their perspectives on activity and pain coping strategies for the management of PDN (Chapters 3 and 5).
5) To conduct an Internet survey investigating which of the impacts of PDN, generated by the patient interview study, respondents would prioritise for better management (Chapter 6).

## *1.7 Researcher perspective*

### *1.7.1 Prior Knowledge*

The researcher had been a full-time clinical physiotherapist in the NHS for twelve years. The majority of this time has been spent in musculoskeletal outpatients, specialising in management of people with persistent pain. The researcher has been involved in delivering multidisciplinary PMPs and physiotherapy-led pain coping skills courses. The pain coping skills courses do not have the expertise of a clinical psychologist involved and the eligibility criteria include mild to moderate depression and anxiety, alongside the pain problem, rather than more severe mood states, where clinical psychology support is more appropriate. The researcher had basic knowledge of DM at the outset of the doctorate and was grateful to learn more about DM and PDN by spending time in tertiary medical clinics for PDN.

### *1.7.2 Thesis worldview*

This thesis focuses on the clinical problem of managing PDN and whether strategies from PMPs would enhance this management. This research takes a pragmatic stance; the focus is on the clinical utility of the outcome rather than the methods involved (Creswell and Plano Clark, 2011). As Chapter 3 will outline in more detail, the overall ontology is constructivist; the researcher will assume that the reality of the person's experience of PDN is contingent on social meaning and internal interpretation, and this experience does not lend itself to simple quantification. There are a variety of qualitative research methods that arise from this stance. The Internet survey (Chapter 6) however, used a quantitative approach to explore and establish patient priorities for management. The approach taken for each study, from research questions to study methods and analysis, was focussed toward improving clinical service provision.

## *1.8 Thesis structure*

Chapter 1 outlined the background to diabetes and PDN, including its current management. It also outlined the content and approach of multidisciplinary PMPs for a range of persistent pain conditions. Chapter 2 presents a systematic review exploring what is currently known about

physical activity and psychological coping strategies for PDN. Chapter 3 describes the methodological considerations for two interview studies, firstly with people who experience PDN, and secondly with clinicians who are involved in helping them manage PDN. Chapters 4 and 5 present the detailed results and discussions for each interview study. Chapter 6 presents an Internet survey that further explored the impact of PDN and the priorities people with PDN had for improved management. Chapter 7 discusses whether the patient priorities identified can be mapped to existing evidence based treatment strategies and where further research is required. Chapter 8 summarises the new knowledge developed by this thesis.

# Chapter 2 – A systematic review of the literature investigating physical activity and psychological coping strategies

*The previous chapter outlined the impact of PDN and the guidance for management, primarily through pharmacology. It introduced the components of PMPs – strategies for physical rehabilitation and for coping psychologically with persistent pain. In this chapter, a systematic review of the literature to establish the evidence for these strategies specifically for people with PDN is presented.*

*A previous version of this study was published in Physiotherapy* (Davies *et al.*, 2015) *and subsequently updated for this thesis (see Appendix 1).*

## *2.1 Introduction*

Multidisciplinary PMPs incorporate various physical activity approaches and a range of psychological models, for example CBT or ACT, but have physical reactivation and psychological coping as their key tenets (BPS, 2013). Multidisciplinary PMPs have a good evidence base for management of non-neuropathic, persistent pain conditions (Main *et al.*, 2012; NICE, 2009; Williams, Eccleston and Morley, 2012).

In the context of chronic pain management, physical activity is not aimed at curing the pain problem but increasing the person's ability to function (BPS, 2013). The physical aspect aims to help people establish a baseline for functional activity and use principles of graded exposure (Boersma *et al.*, 2004) to gradually increase physical capacity. In a recent study (Schneider *et al.*, 2014) of people with PDN (n=2576) the interference that PDN caused to 'general activity' and 'walking ability' were identified as important functions to be improved through treatment for their PDN. These functions are appear appropriate for PMPs, but there is a lack of evidence for any specific form of physical activity in the management of PDN and it is not clear whether activity would alter either pain or function in this condition.

Psychological coping includes the use of cognitive and behavioural interventions to help people live with a persistent pain problem. The authors of a systematic review exploring cognitive and behavioural approaches for neuropathic pain highlighted in their introduction that neuropathic pain is often described by the underlying pathology (for example, PDN), rather than as an entity in itself (van de Wetering *et al.*, 2010). They aimed to devise a search that would accommodate all these pathologies, yet PDN was omitted from the published search strategy. The methodology was subsequently criticised for its heterogeneity in relation to conditions and interventions. Further critique related to the absence of a control arm in 11 of the 14 included

studies and small sample sizes in some studies (Eccleston *et al.*, 2010). Due to these deficiencies, the review by van Wetering *et al.* (2010) was not considered as a definitive state of the literature into psychological coping strategies for neuropathic pain (Eccleston *et al.*, 2010).

Pain, irrespective of cause, is an interfering experience, and reduction in pain severity a common priority of both patients and clinicians (Sanderson *et al.*, 2010; Moore, Derry and Eccleston, 2013). In recent guidance for management of neuropathic pain, NICE note that neuropathic pain has disproportionate effect on physical and mental health than other pain mechanisms, even when adjusted for pain severity (NICE, 2013a). When pain cannot be reduced, a shift of clinical focus to maximisation of quality of life can be appropriate (Smith *et al.*, 2013).

For this systematic review, it was appropriate to set pain severity as the primary outcome as this aligned with patient priorities and studies of medication commonly use this outcome. Selecting pain severity would potentially allow results data from studies investigating physical activity or psychological coping to be compared against treatment effect sizes for medication. Outcomes measuring quality of life were included as secondary outcomes when available in the primary research.

## *2.2 Objectives*

This systematic review had three objectives: to establish the effect of 1) physical activity in the management of PDN, 2) psychological coping strategies in the management of PDN; and 3) identify gaps in the evidence to inform future research priorities for PDN.

## *2.3 Methods*

### *2.3.1 Protocol and registration*

The original protocol was registered with The International prospective register of systematic reviews (PROSPERO) (CRD42013006365), and the study was reported in accordance with the Preferred Reporting Items for Systematic Review recommendations (PRISMA) (Moher *et al.*, 2009).

### *2.3.2 Eligibility criteria*

Studies were required to meet the following inclusion criteria:

1. A study population with a clear diagnosis of painful neuropathy, secondary to diabetes and results reported specifically for people with PDN where individuals with other neuropathic pain pathologies were included in the trial.

2. Human adult participants. PDN becomes more common with longer duration of diabetes; childhood onset is very rare. Basic science studies were inappropriate for investigating utility of clinical interventions.
3. Include an intervention that was either a) physical exercise or activity, and/or b) used recognised psychological approaches that aimed to help participants cope with pain. Studies investigating an intervention that included a combined approach were also included.
4. Patient reported pain as a primary outcome measure.
5. To assess the efficacy of the intervention, only studies using randomised controlled designs were included. The lack of control comparison groups in case series and cohort designs mean changes in outcome measures cannot be assigned to the intervention with any certainty.
6. No exclusion was made based upon language or date of publication.

*2.3.3 Information sources*

Ten electronic databases covering medical, allied health and psychology subjects were searched. The Cochrane Library indexes high quality trials and systematic reviews conducted in healthcare. Physiotherapy Evidence Database (PEDro), Medline/PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Allied and Complementary Medicine (AMED), Embase, SportDiscus, Web of Science and BioMed Central index studies of all methodological designs in healthcare including basic biological sciences and clinical interventions. PsychINFO indexes psychology studies.

*2.3.4 Search*

Symptoms of PDN have a range of clinical diagnostic labels (painful sensory neuropathy, painful distal diabetic neuropathy) and usage of these terms can vary between American and European authors and between pain, diabetes and neurology related journals. Search lines 1-3 in Figure 7 (below) were felt inclusive to ensure any study relating to PDN would be retrieved for consideration.

Existing Cochrane reviews that investigated the effect of physical activity in cancer (Cramp and Byron-Daniel, 2012) and rheumatoid arthritis (Cramp *et al.*, 2013) were used as a basis for this search concept. All approaches to physical training - endurance, strength, flexibility and high-intensity interval training, were included (Figure 7, lines 34-41). These terms were further developed using wild card characters to ensure alternate spellings were not omitted. The search aimed to include physical activity, rather than solely structured exercise, and exercise approaches such as Tai Chi or movement therapy, that do not precisely fit any category. The strategy was

developed (Figure 7, lines 42-44) to include search terms for Neurodynamics (Shacklock, 2007), a manual therapy that mobilizes neural tissue, as this form of activity may have direct relevance to the population with PDN (Boyd, 2008; Boyd *et al.*, 2010), and can be delivered by clinicians or through patient self-mobilization.

For psychological interventions, existing systematic reviews of cognitive behavioural and acceptance based interventions were used as a basis for keyword searches (Veehof *et al.*, 2011; Williams, Eccleston and Morley, 2012). This included established CBT, ACT and MBSR approaches (Morley and Williams, 2015) (Figure 7, lines 5-32).

This search was applied via EBSCO to Medline, AMED, EMBASE, CINAHL, SportDiscus and PsychINFO. A simplified search strategy was used for PEDro, Cochrane Library, BioMed Central and Web of Science. These searches were conducted by the research student in the week beginning 18 November 2013 and repeated 2 July 2014 but limited to studies published in 2013/4 to ensure the results were up-to-date to submit for publication (Davies *et al.*, 2015). To update the review for this thesis, librarian staff at the Royal United Hospitals, Bath, repeated the search in September 2016 limiting dates from 2014 to September 2016.

Figure 7 - Systematic literature review search strategy

1. PAIN explode all trees (MeSH)
2. DIABETES explode all trees (MeSH)
3. Neuropath* or Polyneuropath*
4. **1 AND 2 AND 3**
5. PSYCHOTHERAPY explode tree1 (MeSH)
6. COGNITIVE THERAPY single term (MeSH)
7. BEHAVIOUR THERAPY explode tree 1 (MeSH)
8. BIOFEEDBACK (PSYCHOLOGY) single term (MeSH)
9. ((behaviour* next therapy) or (behaviour* next therapies))
10. ((cognitive next therapy) or (cognitive next therapies))
11. (relax* near technique*)
12. ((relax* near therapy) or (relax* near therapies))
13. meditat*
14. psychotherap*
15. (psychological next treatment)
16. ((psychological next therapy) or (psychological next therapies))
17. (group next therapy)
18. (self-regulation next training)
19. (coping next skill*)
20. (pain-related next thought*)
21. (behavior* near rehabilitat*)
22. (psychoeducation* next group)
23. (psychoeducation* next groups)
24. (psycho-education* next group)
25. (psycho-education* next groups)
26. (mind and (body next relaxation next technique*))
27. MIND-BODY AND RELAXATION TECHNIQUES explode tree 1 (MeSH)
28. mindfulness
29. mindfulness-based stress reduction or MBSR
30. mindfulness-based cognitive therapy or MBCT
31. Acceptance-based or acceptance based
32. Acceptance and commitment
33. **5 OR 6 through 32**
34. ((exercise* or resistance or strength or flexibility or endurance) near (train* or program*))
35. ((resistance or aerobic* or endurance*) near exercise*)
36. (interval training or sport* or movement therap*)
37. stretching.mp
38. (dance therap* or exercise* or “Tai Ji” or “Tai Chi” or “Tai-Ji” or “Tai-Chi” or walking or yoga)
39. graded near (activit* or exercise* or program*)
40. physical* near (active* or therap* or exercise*)
41. exp kinesiotherapy/
42. (nerve or neural) near (glid* or slid*)
43. (nerve or neural) near (exercise* or therap* or treatment* or mobilization*)
44. (nerve or neural) near (tension or mechanic* or dynamic*)
45. **34 OR 35 through 44**
46. **5 AND (33 OR 45)**

*2.3.5 Study selection*

From the studies retrieved, duplicates were removed and the titles judged against the eligibility criteria. Studies that clearly did not meet eligibility criteria were excluded. Abstracts for all remaining studies were then reviewed and judged against the eligibility criteria. The full texts of studies that could not be clearly excluded were obtained. These full texts were judged against eligibility criteria to select the final included studies. In the case of uncertainty, a study was taken forward to the next stage until it was clear it did, or did not meet the criteria. The research student carried out this process.

This process was repeated for the search update conducted in September 2016.

*2.3.6 Data collection process and data items*

The principal data extracted from the selected studies included: evidence of diagnostic criteria for PDN, nature of intervention (type of physical activity, type of psychological therapy), demographics and numbers of the control and intervention arm, duration of follow up periods, outcome measures of pain, results, attrition rates and noted adverse effects. Studies were checked for quality of life outcome measures; if present, appropriate data were extracted at this point. The research student conducted the data extraction using a specific form designed in collaboration with doctoral supervisors (Appendix 2 – Data extraction table). To ensure accuracy Professor Fiona Cramp repeated the data extraction for physical activity studies, and Dr Jeremy Gauntlett-Gilbert for psychological coping studies.

*2.3.7 Critical appraisal and risk of bias in individual studies*

Risk of bias was assessed using the Cochrane Collaboration tool (Higgins *et al.*, 2011) and methodological quality assessed using the NICE critical appraisal tool for randomised studies (NICE, 2006). Although there is overlap in the quality domains of the Cochrane and NICE checklists, both were used to inform an in-depth critical appraisal of the included studies. The Cochrane checklist requires consideration of seven domains where bias can be introduced to a study. Each domain considers whether the research process described by the study authors represents high risk, low risk, or uncertain source of bias. The Cochrane tool does not use scoring scales to quantify the process of critical appraisal.

The NICE checklist guides the reviewer through a series of questions relating to the quality of the methods as well as the results, including their ability to address the study aim(s). The research student reviewed all studies, extracted the necessary information to the data extraction form, and critically appraised the studies. Doctoral supervisors critically appraised the included studies, blind to the opinion of the research student. Professor Cramp performed the second

review for studies involving physical activity and Dr Gauntlett-Gilbert for studies involving psychological interventions. The individual appraisals were compared and discussed in the event of disagreement. A third independent reviewer (Professor McCabe) was available if consensus could not be reached.

## *2.4 Results*

### *2.4.1 Study selection*

After duplicates were removed, 1306 potential studies remained. After excluding studies based on titles, 179 abstracts were reviewed. Reviewing these abstracts against the eligibility criteria left 23 studies for full text review. After final consideration against the eligibility criteria four articles were retained for inclusion in the full review, two studies focused on physical activity and two focused on psychological interventions.

Following the search update in September 2016, 120 articles were retrieved following removal of duplicates. All were excluded based on title or abstract. The outline of the screening process is summarised in Figure 8.

### *2.4.2 Study characteristics (Table 3 - Synopsis of selected studies)*

One quasi-experimental trial of Tai Chi (Ahn and Song, 2012) and one randomised controlled trial investigating aerobic physical exercise (Dixit, Maiya and Shastry, 2014) were included. There were two randomised controlled trials of psychological interventions (CBT and mindfulness relaxation) (Otis *et al.*, 2013; Teixeira, 2010). All participants were diagnosed with either Type 1 or Type 2 diabetes, although the majority had Type 2. Sample size ranged from 19-87, with only two studies reporting a sample size calculation (Ahn and Song, 2012; Teixeira, 2010). The intervention arms were compared with treatment as usual (Ahn and Song, 2012; Dixit, Maiya and Shastry, 2014; Otis *et al.*, 2013) or a control arm of diabetes self-care education that received the equivalent health professional contact time as the intervention arm (Teixeira, 2010).

Figure 8 - Process of study selection

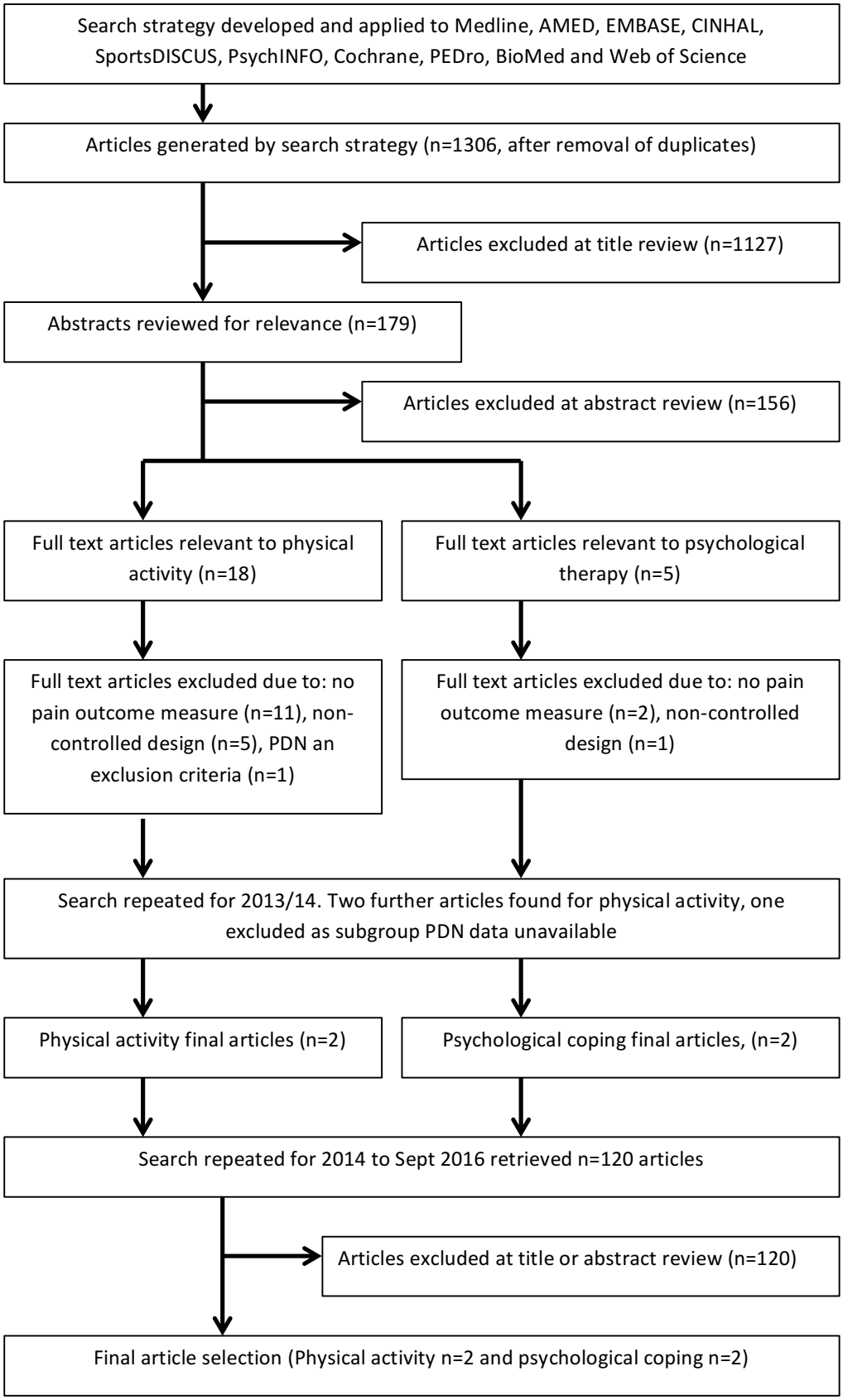


Table 3 - Synopsis of selected studies

| ***Authors*** | **Ahn & Song (2012)** | **Dixit, Maiya and Shastry (2014)** | **Otis *et al.* (2013)** | **Teixeira (2010)** |
|---|---|---|---|---|
| *Research objective* | Physical activity | Physical activity | Psychological coping | Psychological coping |
| *Study design* | Quasi-experimental controlled trial | Single blind, RCT | Single blind, RCT | Single blind, RCT |
| *Participant characteristics*<br>*Mean age (standard deviation)*<br>*Gender*<br>*Type of diabetes*<br>*Duration of diabetes*<br>*Duration of PDN*<br>*Location of treatment* | **Intervention** (n=20): 66 (6.4) years, 12 male, all Type 2, DM duration 12 (8.8) years. PDN duration not stated.<br>**Control** (n=19): 62.7 (7.5) years, 8 male, all Type 2, DM duration -13 (10) years. PDN duration not stated.<br>Korean University Hospital outpatient clinic. | **Intervention** (n=40): 54.4 (1.2) years, 22 male, all Type 2 DM type, DM duration 65.5(1.9) months, PDN duration not stated.<br>**Control** (n=47): 59.4(1.1) years, 31 male, all Type 2 DM, DM duration 82.1(1.6) months, PDN duration not stated.<br>Tertiary care centre, India. | **Intervention**: (n=12): 62 (11) years, all male, all type 2 DM, DM and PDN duration not stated.<br>**Control**: (n=8): 63 (11.6) years, all male, all type 2, DM and PDN duration not stated.<br>USA veterans medical centre. | **All participants** (n=20): 74 (10.8) years, 5 male, all type 2, DM duration 12.6 (9.4) years, PDN duration 7.7 (6.6) years. Community medical practice and retirement communities, USA. |
| *Sample size* | n=39 | n=87 | n=19 | n=20 |
| *PDN diagnostic criteria* | 10g monofilament assessment, Neuropathy total symptom score (TSS) | Physician assessment, Michigan Diabetic Neuropathy Score >7.<br>Other causes for neuropathy excluded | Medical records screened for primary compliant of neuropathic pain in hands or feet | Self-referred, no medical screening |

| ***Authors*** | **Ahn & Song (2012)** | **Dixit, Maiya and Shastry (2014)** | **Otis *et al.* (2013)** | **Teixeira (2010)** |
|---|---|---|---|---|
| *Intervention* | Tai Chi, 2x1 hour per week, 12 weeks, plus routine education on diabetes management | Aerobic exercise at 40-60% of Heart Rate Reserve, 5-6 days per week, accumulating 150-360 mins/week exercise, at Rate Perceived Exertion 6-20. 8 weeks.<br>Advice on foot care and hypoglycaemia | Individual CBT, 1-hour session, x11 sessions. | mindfulness based relaxation (MR), 1 hour session then audio CD for home practice. |
| ***Control arm*** | Routine education on diabetes management | Weekly physician appointments with diet and foot care advice | Treatment as usual, offered CBT after completion of 4 month follow up. | Nutritional advice (1hour) and asked to keep a food diary for 4 weeks |
| ***Outcomes*** | NTSS<br>SF36 (Korean) | MDNS<br>NeuroQoL | WHYMPI<br>BDI | NPS<br>NeuroQoL |

| ***Authors*** | **Ahn & Song (2012)** | **Dixit, Maiya and Shastry (2014)** | **Otis *et al.* (2013)** | **Teixeira (2010)** |
|---|---|---|---|---|
| ***Main statistically significant findings*** | **NTSS**: worsened in both arms but less worse in Tai Chi arm (p=0.042).<br><br>**SF36:** Tai Chi arm improved compared to baseline - Physical function (p=0.028), bodily pain (not neuropathy specific) (p=0.009), physical role limitation (p=0.006) emotional role limitation (p=0.002) and social function (p=0.001). | **MDNS total score** improved in exercise arm 12.57(1.74) (CI 13.11-12.03) to 7.03(1.86) (CI 7.61 – 6.45), control arm 13.55(1.75) (CI 14.05 – 13.05) to 14.57(1.5) (CI 15 - 14.09), p<0.001.<br><br>**NeuroQOL total score** improved in exercise arm, 32.85(1.32) (CI 33.28 – 32.42) to 24.14(1.12) (CI 24.82 – 24), control arm 33.55(1.37) (CI 33.95 – 33.15) to 34.16(1.37) (CI 34.61 – 33.71), p<0.001.<br><br>**NeuroQOL Pain subscale** exercise arm 1.6(1.76) (CI 2.12 – 1.08) to 1.61(1.29) (CI 2.08 – 1.14), control arm 1.65(1.75) (CI 2.17 – 1.14) to 1.73(1.69) (CI 2.28 – 1.18), p=0.03. | **HLM**: CBT arm declined in pain severity (B=-0.54) and pain interference (B=-0.77). TAU arm was not significantly different. No change in BDI either arm.<br><br>**Pre-post (4/12) for CBT arm**: pain interference decline t(7)=3.15, p<0.5, pain severity declined t(7)=3.87, p<0.1. 2/8 CBT arm 50% reduction in pain, 3/8 at least 20% reduction in pain.<br><br>**Between arm pre-post (4/12)**: pain severity decreased 1.08 (sd 0.79), TAU unchanged, p<0.1, Pain interference CBT declined 1.35 (SD 1.22), TAU increased 0.22 (SD 0.73) p<0.5 | **Hypothesis 1** (MR leads to QoL improvement): no significant difference in overall QoL, symptom related QoL, pain QoL or emotional QoL.<br><br>**Hypothesis 2** (MR leads to decreased pain): no significant difference in pain intensity or pain unpleasantness. |
| ***Adverse effects/events*** | None noted | Not reported | Not reported | Not reported |

BDI – Beck depression inventory, CBT – Cognitive behavioural therapy, DM – Diabetes mellitus, HLM – Hierarchical linear modelling, HRR – Heart rate reserve, MR – mindfulness relaxation, MDNS – Michigan diabetic neuropathy scale, NPS - Neuropathic pain scale, NTSS - Neuropathy total symptom score, PDN – Painful diabetic neuropathy, QoL – quality of life, RCT – randomised controlled trial, RPE – rate of perceived exertion, SF36 – Shortform 36 health survey, TAU – treatment as usual, WHYMPI - West Haven Yale Multidimensional Pain Inventory

*2.4.3 Risk of bias and quality appraisal*

The summary of the Cochrane and NICE appraisal checklist can be found in Table 4 and Table 5 respectively. The relevant methodological issues in each study will be reviewed in turn.

Table 4 - Cochrane Risk of bias assessment (Higgins *et al.*, 2011)

| | **Ahn & Song (2012)** | **Dixit, Maiya and Shastry (2014)** | **Otis *et al.* (2013)** | **Teixeira (2010)** |
|---|---|---|---|---|
| ***Random sequence allocation*** | + | - | - | - |
| ***Allocation concealment*** | + | + | + | ? |
| ***Blinding of participants and personnel*** | + | + | ? | + |
| ***Blinding of outcome assessment*** | ? | - | ? | ? |
| ***Incomplete outcome data*** | + | + | + | ? |
| ***Selective reporting*** | - | - | ? | - |
| ***Other bias*** | ? | + Low recruitment % | ? | ? |
| *+* High *risk of bias, - low risk of bias, ? risk of bias cannot be ascertained* | | | | |

Table 5 - Assessment of methodological quality checklist 1.1 – 2.3 (NICE, 2005)

| | **Ahn & Song (2012)** | **Dixit, Maiya and Shastry (2014)** | **Otis *et al.* (2013)** | **Teixeira (2010)** |
|---|---|---|---|---|
| ***Clear research question*** | Adequately addressed | Well covered | Well covered | Well covered |
| ***Randomization process*** | Poorly addressed | Well covered | Well covered | Well covered |
| ***Adequate concealment*** | Not applicable | Not addressed | Not addressed | Not addressed |
| ***Subjects and investigators 'blind'*** | Not addressed | Poorly addressed | Not reported | Poorly addressed |
| ***Similar pre-trial intervention and control arms*** | Well covered | Well covered | Adequately addressed | Not addressed |
| ***Intervention is only difference between arms*** | Well covered | Well covered | Well covered | Adequately addressed |
| ***Valid and reliable outcome measures*** | Adequately addressed | Well covered | Well covered | Well covered |
| ***Dropout rates prior to completion*** | Well covered | Well covered | Well covered | Well covered |
| ***Intention to treat analysis performed*** | Not addressed | Not addressed | Not addressed | Not addressed |
| ***Comparable between sites*** | Not applicable | Not applicable | Not applicable | Not applicable |
| ***How well does method minimise bias?*** | - (Not randomized or blinded) | + (Lost data from those whose pain increased, lost motivation, other reasons) | + (Not blinded, lost data from drop outs) | - (Not blinded, did not achieve sample size) |

| | Ahn & Song (2012) | Dixit, Maiya and Shastry (2014) | Otis *et al.* (2013) | Teixeira (2010) |
|---|---|---|---|---|
| ***If biased, in which direction?*** | Likely overestimate the benefit of intervention | Likely overestimate the benefit of intervention | Likely overestimate the benefit of intervention | Likely overestimate the benefit of intervention |
| ***Considering clinical aspects, method and statistics, is the overall effect due to intervention?*** | Moderately | Uncertain, intervention arm unchanged clinically, control arm worsened, leading to the statistical significance | Moderately | Uncertain |

Ahn & Song (2012) conducted a quasi-experimental study investigating the effects of Tai Chi. The first thirty participants consented were allocated Tai Chi, and their outcomes compared to the next block of twenty-nine control participants. A sample size calculation was conducted based on the ability to detect change in HbA1c, and the target sample was recruited. Although not true randomisation there were no significant differences between study arms at baseline for the sociodemographic and clinical variables recorded. The authors used a robust range of outcome measures but they do not state clearly if these were completed by researchers blind to treatment allocation. The study suffered from a high drop-out rate (~30%) in both study arms and the management of missing data was not discussed, so the results are at risk of attrition bias.

Dixit, Maiya and Shastry (2014) investigated structured aerobic exercise. They stratified the severity of the neuropathy using the Michigan Diabetic Neuropathy Score and then randomised participants into study arms accounting for equal severity of the neuropathy. There were clear protocols for minimising allocation and detection bias, through blinding of researchers to the trial arm of participants. Anthropometrics were shown to be similar between trial arms at baseline, but other characteristics were not analysed. Clear details of the intervention were provided, and the comparison arm received weekly physician appointments. Such frequency may not represent true 'treatment as usual'. No sample size calculation was conducted, however the researchers assessed n=335 potential participants and recruited n=87, highlighting difficulties in recruitment from their population. There was significant loss to follow up (~22%) in both arms of the trial and no details were provided of how missing data were managed so the results are again at risk of attrition bias.

Teixeira studied the effect of mindfulness relaxation on PDN (Teixeira, 2010). They used random number draw to allocate participants to trial arm and used outcome measures for quality of life (NeuroQoL) and pain (Neuropathic Pain Scale) that have been validated for neuropathic

pain. Previous studies informed a sample size calculation, however the target was not achieved allowing the possibility of type II error. Further, it is not clear that the arms were equitable at the start of the trial or that researchers were fully blind to the treatment arm, allowing for potential detection bias. There was minimal loss to follow up but it is not clear how the missing data were handled.

Otis *et al.* (2013) conducted a pilot trial of CBT in a US military veteran population. Participants were randomised to trial arm and these were demonstrated to be comparable at baseline for the sociodemographic variables recorded. The CBT intervention was clearly outlined. The study used the WHYMPI as their primary outcome measure, which has not been validated for neuropathic pain. It was not clear that researchers responsible for outcome measures were fully blind to the treatment arm. Outcomes were reported for three time points (pre-, post-course and at three months), and appropriate statistical analysis was used to account for repeated measures, but caution should be applied due to the small sample size (n=19) and significant attrition in the treatment arm (3 of 11, 27%).

Overall, few studies were located and each of the studies investigated a different form of physical exercise or psychological coping. These studies defined their participant eligibility criteria, used appropriate outcome measures for pain or quality of life in persistent pain states, and described the interventions clearly. These studies were all of small sample size; either not stating a sample size calculation, or not retaining the sample size to the end of the study. Studies experienced difficulty in recruiting participants to, or retaining participants within the studies. In general, appropriate steps had been taken to blind researchers, but for the interventions studied it was impossible to achieve true blinding of participants. The main concerns with all the identified studies were high attrition rates and the lack of clear intention to treat analysis; this allows results potentially to be inflated in favour of the interventions.

### *2.4.4 Results of individual studies*

Detailed results can be found in Table 3 - Synopsis of selected studies.

#### *2.4.4.1 Primary outcome measure*

Ahn & Song (2012) used the SF36 and Neuropathy Symptom Score outcome measures. The SF36 bodily pain subscale improved in the intervention arm from pre- to post-intervention by mean difference 11.87 (SD26.74) and worsened in the control arm by mean difference -11.34 (SD6.17) (post-intervention between arm comparison p=0.009). The Neuropathy Symptom Score contained questions related to pain and function but the individual pain data were not specified in the results. Overall the Neuropathy Symptom Score improved slightly in the intervention arm

(mean difference 0.21 (SD1.44)) and worsened in the control arm (mean difference -1.64 (SD3.61)), post-intervention between arm comparison p=0.042. The sample size calculation was based on ability to detect changes in HbA1c, not changes in pain, and therefore it is unknown whether the study was powered appropriately when considering results related to pain experience.

Dixit, Maiya and Shastry (2014) used the NeuroQOL measure that contains a specific pain subscale. They demonstrated minimal change in the intervention arm (mean 1.60 (SD1.76) to 1.61 (SD1.29)) and worsening pain in the control arm (mean 1.65 (SD1.75) to 1.73 (SD1.69)), post-intervention between arm comparison (p=0.03).

Otis *et al.* (2013) used the WHYMPI as the pain outcome measure. Hierarchical linear modelling was used to analyse the data and account for repeated measures. Analysis showed the CBT group decreased in pain severity (B=-0.54) and pain interference (B=-0.77). There were no significant changes in the treatment-as-usual arm. From pre-intervention to 4 month follow up pain severity decreased in the CBT arm and did not alter significantly in the treatment-as-usual arm ($p<0.01$). Pain interference also decreased in the CBT group compared to the treatment-as-usual arm ($p<0.05$).

Teixeira (2010) proposed two hypotheses within their study: 1) mindfulness relaxation leads to quality of life improvement and 2) mindfulness relaxation leads to decreased pain. The results demonstrated no difference between intervention and control arms for either hypothesis.

Only Ahn & Song (2012) specifically reported on monitoring for adverse effects with no events in either arm. No other included study specifically stated the occurrence of adverse events.

*2.4.4.2 Secondary outcome measures*

The SF36 questionnaire used by Ahn & Song (2012) includes subscales for physical role and emotional role, amongst others. Table 6 summarizes selected results. For the intervention arm there were improvements in several quality of life subscales, but there were deteriorations in these measures for the control arm.

Table 6 - Selected results SF36 (Ahn & Song 2012)

| | **Tai Chi – pre-post mean difference (SD), n=20** | **Control – pre-post mean difference (SD), n=19** | **p=** |
|---|---|---|---|
| ***Physical function*** | 4.75(16.58) | -5.78(11.69) | 0.028 |
| ***Role physical*** | 17.25(28.64) | -4.02(14.20) | 0.006 |
| ***Role emotional*** | 17.5(24.78) | -7.36(20.73) | 0.002 |
| ***Social function*** | 10.89(30.29) | -18.28(18.85) | 0.001 |

The NeuroQoL measure used by Dixit, Maiya and Shastry (2014) included the overall pain score, reported earlier, and subscales for quality of life. Selected data were presented in Table 7. As with the results in the previous paragraph, while the intervention arm had improved for a number of quality of life subscales, this was accompanied by reduction in these scores for the control arm.

Table 7 - Selected results NeuroQoL (Dixit, Maiya and Shastry, 2014)

| | **Aerobic exercise (absolute % change), n=29** | **Control (absolute % change), n=37** | **p=** |
|---|---|---|---|
| ***Restricted activity daily life*** | 23.21 | -4.14 | 0.03 |
| ***Disruptions in social relationships*** | 21.73 | -28 | 0.02 |
| ***Emotional distress*** | 11.31 | -14.82 | 0.10 |
| ***Specific impact on QoL*** | 16.67 | -1.67 | <0.001 |
| ***Overall QoL score*** | 19.64 | -14.26 | <0.001 |
| *QoL – quality of life* | | | |

In the remaining studies, Otis *et al.* (2013) used the WHYMPI measure, which comprises 12 subscales but they only consider the Pain Interference and Pain Severity subscales in their analysis, and did not present other subscale data. Teixeira (2010) used the NeuroQoL measure, but did not present the subscales in a manner that allowed interpretation.

### *2.4.5 Synthesis of results*

Physical activity appeared to benefit general quality of life, as rated by SF36 and NeuroQoL measures, rather than pain specifically. Where there were statistically significant effects on pain, it appeared that pain increased in control arms, rather than pain improving in the intervention arms. There appeared to be significant barriers to recruitment and retention in physical activity studies. CBT appeared to benefit participants, but dropouts occurred early in the intervention. These results need to be considered with some caution given the small sample size and high attrition rates in most studies.

## *2.5 Discussion*

This systematic review aimed to examine the evidence for physical activity and psychological coping strategies in the management of PDN. Two studies of physical activity and two studies of psychological therapy were identified. The identified studies were heterogeneous with methodological limitations. The findings suggest that physical activity has the potential to improve overall physical and mental wellbeing, and possibly to arrest an increase in pain compared to control arms. In the one study that reported adverse effects (Ahn and Song, 2012),

none were noted beyond transient pain increases or hypoglycaemia. Mindfulness relaxation did not have a significant effect on pain or quality of life, though the intervention studied involved very little actual contact time with a professional. CBT was shown to improve pain and quality of life in a single study, but this was a small pilot study that was significantly affected by participant dropout.

### *2.5.1 Physical activity for PDN and DM*

From the studies that investigated physical activity, Ahn & Song (2012) demonstrated improvements in SF36 subscales in the intervention arm, though this might be due to improvement in general physical and emotional health, as much as impact on PDN specifically. There was inconclusive evidence regarding the impact on pain; in fact it appeared the significant findings in Ahn & Song (2012) and Dixit, Maiya and Shastry (2014) were due to control arms worsening rather than intervention arms improving. It maybe that people with PDN need to be more active (physically) in order to stand still (in terms of pain).

There are known methodological difficulties using pain self-report measures to objectify a subjective experience (Moore, 2013). Attention toward an experience, in order to rate it, can often increase the pain severity (McCabe *et al.*, 2005; van Damme *et al.*, 2009). This attention can lead to bias in the reporting of pain experience both at the pre- and post-intervention stages of an intervention trial. However, these rating scales, whether VAS or NRS, have been used in the majority of pain research to represent an outcome of importance to patients with PDN (Schneider *et al.*, 2014).

The eligibility criteria for this review specified the inclusion of pain severity as an outcome within the included studies. Other measures of function or quality of life were included as secondary outcomes of the review where reported. This study was not designed to locate all studies that investigated the effect of physical activity on quality of life in PDN. Although the results presented here do suggest engagement in physical activity may have positive effects on PDN-related quality of life, this cannot be made with certainty at this point. The review results were broadly congruent with a recent Cochrane overview of physical activity for chronic pain, which found inconsistent results for changes in pain severity but more consistent improvements in measures of physical function (Geneen *et al.*, 2017).

Considering diabetes more generally, public health research clearly demonstrate that increasingly sedentary behaviours and changing diets are contributing to the rising prevalence of the condition (Department of Health, 2010a; Alberti and Zimmet, 2013). There are few extrinsic barriers to most adults achieving the recommended levels of physical activity (Department of

Health, 2010a, 2011); rather internal motivation to increase and sustain activity levels is shown to be a limiting factor (Sørensen, Skovgaard and Puggaard, 2006). Irrespective of whether physical activity has benefits to PDN for pain reduction or quality of life increase, physical activity has positive benefits for managing diabetes.

The DARE (Diabetes Aerobic and Resistance Exercise) trial evaluated the effectiveness of aerobic and/or resistance exercise compared to a control arm, for improving glycaemic control and so reducing the risk of macrovascular and microvascular complications of DM (Sigal *et al.*, 2007). The study (n=251 adults with T2DM) found combined exercise (n=64, aerobic and resistance, 3x/week, 22 weeks) reduced HbA1c by -0.51% (CI -0.87 to -0.14) compared to the control arm (n=63, p-0.007 between group comparison). Aerobic and resistance exercise were also beneficial compared to control arm, but less so than a combination of both. A later health economic evaluation also found the increased investment in delivering the combined exercise programme (Canadian $40,050, control $31,075) cost effective for increasing quality adjusted life years (QALYs) (Combined exercise $4792/QALYs, control $37,872/QALYs) (Coyle *et al.*, 2012). Such research highlights that strategies to increase physical activity in people with diabetes have health benefits for other aspects of DM, if not yet demonstrated for PDN.

The low recruitment and high attrition rates within the studies included in this review suggest recruitment and retention to physical activity programmes needs further research to inform the development of clinical services. Further research is required to understand the patients' perceptions of physical activity, what potential benefits they consider and what barriers maybe present to them accessing physical activity.

*2.5.2 Psychological interventions for PDN*

The psychological coping interventions studied were CBT (Otis *et al.*, 2013) and mindfulness relaxation (Teixeira, 2010). There was insufficient evidence from these studies to make recommendations on these approaches for PDN. While the results from Otis *et al.* (2013) appear encouraging, the high dropout rate limits the findings. The authors note the dropouts occurred by session three of eleven. One possible explanation is lack of 'buy-in' to CBT lead to early dropout. Guidance from the British Pain Society stresses that engagement with PMPs cannot be coerced (BPS, 2013) and assessment must be made of the person's readiness to adopt alternative physical and psychological behaviours. It is possible the participants who dropped out from CBT conceive their pain as due to nerve damage or disease related processes, and view psychological treatment as irrelevant to their pain experience (Martin, Daniel and Williams, 2014).

As noted in section 2.1, the only existing systematic review for psychological interventions in neuropathic pain, van de Wetering *et al.* (2010), had been heavily criticized (Eccleston *et al.*, 2010). In order to address these criticisms, the Cochrane Collaboration conducted a systematic review for psychological therapies in neuropathic pain (Eccleston, Hearn and Williams, 2015). Eccleston, Hearn and Williams, (2015) only included studies of randomised and controlled design; the intervention had to be based on recognised psychological approaches and retain a minimum 20 participants in each arm at follow-up. Trials with small sample sizes are at risk of over-estimating the effects of treatment because of regression to the mean, amongst other sources of bias (Moore *et al.*, 2010). The review identified two studies for inclusion: CBT for pain in spinal cord injury (Heutink *et al.*, 2012) and psychotherapy in 'Burning mouth syndrome' (Miziara *et al.*, 2009), neither of which demonstrated beneficial effects. The two psychological intervention studies included in this current review would have been excluded on the criterion of insufficient sample size. At the time of developing the search protocol used for this chapter (2013), the Cochrane review had not been published; the aim of this chapter was to find all published research specific to PDN, so no lower sample size limit was set. Since both these reviews found little published evidence, it is clear there is currently a scarcity of research into management of the impact of neuropathic pain by psychologically directed interventions.

### *2.5.3 Further research*

The population who experience DM and PDN is increasing (Alberti and Zimmet, 2013). PDN impacts on many day-to-day functions such as activity and walking, and is distressing (Alleman *et al.*, 2015). The available analgesics are not sufficient to ameliorate these impacts (Finnerup *et al.*, 2015), and there is a lack of concordance between the range of impacts and the current management approaches for PDN. As health services reconfigure to deal with the increasing burden of chronic diseases such as diabetes, pain management services may come under increasing pressure to help manage this condition. Currently the evidence base for the two key pillars of PMPs is scarce and of low quality.

NICE highlight that neuropathic pain has greater effect on quality of life than other pain conditions even when pain severity is controlled for, and it is unclear what other factors are responsible for mediating quality of life (NICE, 2013a). NICE (2013a) recommended in-depth qualitative research with people who experience neuropathic pain to elucidate factors deemed important to improve their quality of life.

Research trials into physical activity had difficulty recruiting and retaining participants. It would be profitable to explore peoples' opinions of physical activity, to understand issues of engagement and motivation for physical approaches. Similarly, the one study with CBT had

significant participant drop out, early in the intervention. (Otis *et al.* 2013). It would be beneficial to understand whether people with PDN view psychological interventions as appropriate and relevant to the problems they have to manage.

The perspective of clinicians to these strategies was also considered important to explore. The clinical opinion diabetes clinicians have for PMP strategies would affect the likelihood of them endorsing and referring their patients with PDN to pain services for management. The perspective of pain clinicians was also important, to understand whether they felt people with PDN could fit into existing pain services, or, if necessary, what alterations might be required.

The explorative nature of these questions best suits qualitative approaches (Petty, Thomson and Stew, 2012a). The methodology and methods used for both these qualitative studies are described in the following Chapter 3, with results for patients detailed in Chapter 4, and clinicians detailed in Chapter 5.

### *2.6 Conclusions*

A central tenet of PMPs aims to assist people to improve their physical capacity. The two studies investigating physical activity contain significant methodological bias, notably high participant attrition rate lost to follow up.

The other tenet of PMPs is psychological coping, yet the paucity of the studies retrieved does not allow firm conclusions to be made on the best psychological strategies to help people to cope with their persistent pain.

*The next chapter will detail the methodological considerations for two interview studies, with people who experience PDN and with clinicians who are involved in its management. The chapter will detail the philosophical approach with the inherent assumptions that are then present, and will detail the methods used for these studies.*

# Chapter 3 – Methodology and methods: patient and clinician interviews

*This chapter opens by considering what attributes are necessary for quality and rigour in qualitative research. The philosophical position and methodological considerations for the interview studies are then examined. The nature of the experience being investigated (living with PDN), the rationale for using specific research methods (one to one interviews) and the analytical framework used (thematic analysis) are then considered. The methods used to recruit participants and collect the data are subsequently provided. Justification is also provided for the research methods with consideration of the strengths and limitations of the approach.*

## *3.1 What constitutes high quality qualitative research?*

The products of research should not be accepted blindly, but rather, considered critically. This means considering whether the research process is likely to have produced results and conclusions that can be considered 'true'. The standards for critical appraisal depend on the ontological and epistemological perspectives of the research (Mays and Pope, 2000; Pope and Mays, 2006). These standards need to be considered by the researcher when designing the research study and collecting data, as well as when producing dissemination reports. These standards must also be considered by research consumers who will critically appraise the research produced, in order to consider the implications for their clinical practice (Katrak *et al.*, 2004).

Research produced within a quantitative framework should provide results that are valid and reliable. This means valid results accurately reflect the reality of the phenomena being investigated. Reliable results are those shown to be repeatable and so generalizable from the study sample, to the wider population.

The application of terms, such as validity and reliability, to qualitative research has been disputed. Authors contend that attempts to use these terms for quality appraisal in a qualitative framework, force this type of research to be measured against inappropriate goal posts (Yardley, 2000; Sandelowski and Barroso, 2002; Rolfe, 2006). The underlying philosophical positions of qualitative research are that phenomena, particularly social and personal experience, are dependent on a variety of factors, and there is not one universal 'truth'. It is inappropriate to ask whether a qualitative research study has 'valid' conclusions, since there is no assumption that a 'true' result exists. Equally, it is not appropriate to expect to obtain similar results by repeating a qualitative research study, as the small sample group and differing sociocultural factors involved would inevitably mean conclusions could differ (Yardley, 2000; Rolfe, 2006).

This does not mean qualitative research is not worthwhile *per se*, rather the consumer of the research must consider if the research context is applicable to their clinical area. For clinical health research this means considering whether the social and cultural variables in the research population mirror those variables in the clinical population in which the research consumer works. When considering the quality of qualitative research, it is important to have transparency of the contextual and situational settings, as well as the clinical profile of the participants. Research consumers must also consider whether the study methods used, are an appropriate match between research questions and the stated conclusions (Pope, Ziebland and Mays, 2000).

In the following sections the methodological considerations for each interview study will be considered separately or together, as needed for clarity. Strategies that were used to develop and maintain quality research will be outlined in appropriate sections.

### *3.1.1 How is research quality appraised?*

The strategies used to assure research quality in qualitative studies has been the subject of a review (Reynolds *et al.*, 2011). Reynolds *et al.* (2011) highlight two narratives in the literature: that quality appears to be demonstrated either by reflection on the research process over the lifespan of the project – *Process orientated quality assurance*, or at the point of research dissemination – *Output orientated quality assurance*.

The process-orientated option relies on transparency at key decision points on the project journey, reflections on interpretation throughout the analysis and a demonstration of researcher engagement with these processes. The following methodological sections will describe these decisions and the procedures in place to ensure research quality through data gathering and subsequent analysis.

It is the author's responsibility to include sufficient detail of the sample demographics, recruitment and analytic assumptions amongst other details, so that the research consumer can evaluate trustworthiness. Within quantitative research, checklists have been established to help the consumer consider quality - NICE and the Scottish Intercollegiate Guidelines Network are two cited examples. A systematic review of existing checklists for qualitative research found 22 in existence, suggesting uncertainty regarding quality appraisal of qualitative research (Tong, Sainsbury and Craig, 2007).

The review by Tong, Sainsbury and Craig (2007) led to the Consolidated criteria for Reporting Qualitative research (COREQ), a 32-item checklist that was created using expert consensus to combine existing checklists and consolidate them into three domains: Domain 1 – research team and reflexivity, Domain 2 – study design and Domain 3 – analysis and findings. The

COREQ checklist aims to help the consumer critically evaluate the presented research, in order to evaluate the methodological strength and the utility of the results in their clinical work. This checklist has been used when writing Chapters 3, 4 and 5 to ensure that the studies were presented with sufficient detail to allow full critical appraisal. Importantly, as with checklists for quantitative research, the COREQ checklist does not rate the quality of the research directly, but provides a critical framework for use by the research consumer to decide upon the quality and applicability.

## *3.2 Introduction to patient study*

Currently the management of PDN is nearly entirely pharmacological (Bril *et al.*, 2011; NICE, 2013a), yet patient satisfaction with the effectiveness of these medication strategies has been low (Gore *et al.*, 2006; Sadosky, Hopper and Parsons, 2014).

While PMPs have been shown to be clinically effective (Williams, Eccleston and Morley, 2012; Phillips *et al.*, 2008), the effectiveness cannot be assumed to transfer to other populations with distinct pathologies (Turk and Okifuji, 2001). PMPs are delivered to people who have persistent pain of any cause, yet because of the differences in neuropathic pain outlined in Section 1.5.3, it may be appropriate to refine the content of PMPs specifically for neuropathic pain problems.

No research to date has asked people with PDN how they currently manage impacts with the potential that personal experience may hold useful information to inform coping strategies. It is unknown whether people with PDN would find adjunctive pain management strategies, particularly physical and psychological approaches, to be acceptable or appropriate for the impacts of PDN.

### *3.2.1 Patient study aims*

The patient interview aimed to explore: 1) how PDN impacts on participants' lives, 2) the strategies participants have developed to manage these impacts, 3) the participants' perspectives on the potential utility of PMP strategies for coping with persistent pain.

### *3.2.2 Patient study objectives*

The objective of this study was to conduct one-to-one interviews, either in person or by telephone, with people who experience PDN.

### *3.2.3 Patient study research questions*

1) What are the impacts of PDN on the participant's life?
2) What strategies do participants employ to manage the impact of PDN on their lives?

3) What are their views on physical activity strategies to manage the impact of PDN?
4) What are their views on pain coping strategies to manage the impact of PDN?
5) How do people who may have multiple diabetic co-morbidities prioritise the management of their health issues?

*3.3 Introduction to clinician study*

The symptoms of PDN and consequent functional limitations, are under-reported by patients and not routinely inquired about by health care professionals (HCP) (Sadosky, Hopper and Parsons, 2014). General Practitioners (GPs) and diabetic specialist nurses (DSN) have the principal responsibility for managing diabetes in primary care (Department of Health, 2010b); only patients with more complex medical requirements should be referred on and managed in secondary care clinics (Department of Health, 2010b; NHS BNSSG, 2012). Diabetes can lead to a range of secondary complications which means a person could be under the care of many different specialities concurrently for example: renal, cardiovascular, vascular, and ophthalmology clinics.

In England, the QOF directs primary care management of diabetes. It stipulates the need to gather specific data from patients and provide specific clinical services to improve care. There are financial incentives for primary care practices that comply with this guidance. The QOF system for 2016/17 included targets for management of glycaemic control, hypertension, regular foot assessment and enhancing self-management. Foot assessment was retained, aiming to identify patients at risk of diabetic ulcers and potential amputations. There were no QOF indicators for the management of pain related to diabetes (NHS Employers, 2016) resulting in a lack of external incentive for clinicians to ask about this type of pain.

Discrepancies have been identified between patient and HCP experiences of PDN assessment. Daousi *et al.* (2004) found 13% of their population with PDN had never reported their pain symptoms to a HCP and 39% had never received any form of treatment. More recently, Sadosky, Hopper and Parsons (2014) found 83% of the patient population reported pain consistent with PDN, but only 41% had received an official diagnosis, suggesting that PDN may remain under diagnosed and managed. When symptoms were raised, 72% of patients felt their pain was only discussed 'in passing', yet 45% of HCP felt these discussions were 'in detail' (Sadosky, Hopper and Parsons, 2014). Potential barriers to communication included difficulty for patients in describing their symptoms and the perception that the presence of pain indicated poor diabetes management (Sadosky, Hopper and Parsons, 2014). Taylor-Stokes *et al.* (2011) found HCPs underestimated pain intensity compared to patient reports in nearly half of cases.

When pain is raised, the recommended management is entirely based on medication, see Chapter 1, section 1.3 for details. These medication strategies have NNT between four and eight, which leaves many people with sub-optimally managed pain and related distress. A recent survey of 500 clinicians who treated people with PDN (50% GPs, 30% specialist physicians including diabetologists and pain clinicians, 20% nurses) found 87% wanted more information on non-pharmacological strategies they could employ or recommend to their patients with PDN (Sadosky, Hopper and Parsons, 2014). This suggests that clinicians are mindful that medication lacks efficacy and have identified a need for adjunctive strategies.

If adequate pain control cannot be achieved with medication, the guidance documents suggest onward referral to secondary pain services. An audit of UK national pain services found patients with pain classified as neuropathic accounted for 856 of 9528 (9%) patient contacts (BPS, 2012). Examination of the ICD-10 classification (International Statistical Classification of Diseases and Related Health Problems, World Health Organisation) assigned by clinicians to their patient cases, found musculoskeletal pain accounted for 67% of classifications and codes related to PDN were not present in the top-25 frequently used codes (BPS, 2012). The British Pain Society report specifically highlighted that neuropathic pain appears under-represented in pain clinics.

Patients are usually referred to PMPs from pain clinics, rather than direct access; therefore, if neuropathic pain were under-represented in pain clinic, it is likely under-represented in PMPs. The experience of pain clinicians who have treated people with neuropathic pain in PMPs, suggest these patients appear to require adapted packages of PMP components, rather than those traditionally delivered for musculoskeletal pain (Daniel *et al.*, 2015). They suggest the differences in the symptom profile and impact between musculoskeletal pain and neuropathic pain make certain common approaches to pain, such as pacing, unsuccessful or irrelevant to patients with neuropathic pain (Daniel and Van der Merwe, 2006; Daniel *et al.*, 2007). Research has highlighted the range of opinions held by patients with neuropathic pain when considering the interaction of psychology and pain, and whether psychological therapy was considered appropriate (Martin, Daniel and Williams, 2014). These were discussed in detail in Chapter 1, section 1.5.3.

Section 1.6 highlighted that the patient perspectives on PMP strategies were largely unknown. The perspectives of clinicians involved in diabetes and pain management to using pain management strategies with neuropathic pain, were also unknown. Diabetes clinicians play a central role in managing PDN and potentially referring onto other services to help their patients manage PDN. Pain clinicians have experience of applying PMP strategies with a variety of pain conditions and may have valuable clinical insight.

*3.3.1 Clinician study aims*

The clinician interview study aimed to understand clinicians' approaches to the management of PDN and their views on whether physical activity and psychological coping strategies might be appropriate for this population. It used their experience of diabetes, PDN and pain management to understand how the content and delivery of PMPs may need to be tailored to this patient group.

*3.3.2 Clinician study objectives*

The objective was to conduct one-to-one interviews with a range of clinicians who were primary care generalists, or specialist in managing diabetes or pain.

*3.3.3 Clinician study research questions*

1) How do clinicians involved in diabetes management, currently help patients to manage PDN?
2) What are clinician's perspectives on the usefulness of physical activity as a means to manage PDN?
3) What are clinician's perspectives on the usefulness of psychologically based pain coping strategies as a means to manage PDN?

*3.4 Research methodology*

*3.4.1 Patient study – Ontology*

Ontology is the philosophical study into, and questions about the reality of nature and existence. It asks questions about Truth and Being, that is, what can be said to exist (Petty, Thomson and Stew, 2012a).

There are two opposed views on the nature of truth – the positivist paradigm proposes there is truth present in the world, which can be discovered with hypothesis generation and tested with objective experimental research designs. These designs provide numerical data that will either support or refute the hypothesis. Post-positivism, in contrast with Positivism, accept empirical data have an element of error and so the absolute truth of reality may not be described by experimentation. The Interpretivist paradigm posits that some truths, such as personal experience, are not quantifiable, so these experiences cannot be reduced to numerical data because the personal experience is effected by social context, personal beliefs and psychological variables (Cutcliffe and McKenna, 2002; Petty, Thomson and Stew, 2012a, 2012b). The experience of pain could be investigated under both paradigms, so the appropriate method must be selected to answer the specific research questions.

The personal subjective experience of 'pain' is an emergent neurocognitive event that arises from the interactions of multiple body systems including the peripheral nervous system, spinal cord, multiple brain areas, the immune and endocrine systems (Thacker and Moseley, 2012; Quintner *et al.*, 2008; Thacker, 2015). In this context, the term 'emergent' highlights that the experience of pain - what it is like for that person - is not a linear process located in pain pathways and pain centres as suggested by René Descartes (Cohen *et al.*, 2011), but a dynamic process dependent upon many variables (Chi *et al.*, 2012). Conceptual models such as the MOM (Gifford, 1998a) and the Neuromatrix Theory (Melzack, 1999, 2001) highlight the breadth of factors that must be considered to begin to understand pain. Psychological factors such as fear of (re)injury (Vlaeyen and Linton, 2000), raised worry about pain severity (catastrophization) or potential futures with pain (Turner, Jensen and Romano, 2000), and emotional distress (Campbell, Clauw and Keefe, 2003) have been demonstrated to affect the impact any structural pathology may have on a person's experience. In addition, the social environment a person lives in and their social support networks have been demonstrated to affect the perceived impact of pain (Kendal, Linton and Main, 1997). The social environment also has an effect on management of diabetes, with greater social support associated with improved outcomes and positive changes in lifestyle (Strom and Egede, 2012).

The patient study aimed to explore the impact of PDN on the person and how they managed that impact - the experience or *phenomenon* of living with and managing PDN. Due to the wide range of psychological and other variables described earlier, research methods that used an Interpretivist ontological paradigm were most appropriate to answer the research questions. These questions do not have a predetermined expectation of what might be found. There is no stated hypothesis; rather, they aim to explore the personal experience of participants. Such exploratory questions demand a qualitative approach (Smith, Bekker and Cheater, 2011). It would not be appropriate to use post-positivist research methods such as questionnaires with closed-ended questions. The construction of a questionnaire by researchers who have no experience of the problem and imperfect knowledge of the condition would limit the participant's potential responses. Questionnaires could have been constructed with open-ended questions which would have allowed participants to report discursively about their experiences (Yardley, 2000). This approach would however have prevented the interviewer from interacting with the participant to ensure as clear an understanding as possible, of their responses.

### *3.4.2 Patient study – Epistemology*

Epistemology is the philosophical perspective on ways by which we can acquire knowledge. There must be concordance between ontology and epistemology for any research programme to

be coherent (Carter and Little, 2007). Since the ontological perspective is Interpretivist – the subjective experience of the participants is created by their interpretation of many variables – it would not be concordant to take objective measures such as walking speed or body temperature to be an accurate representation of their experience. This research programme accepts the experience of participants is constructed by their thoughts, beliefs, and social world – a social constructionist epistemological position. People with PDN are best placed to relate that phenomenon within the research process through their spoken words. It is important that no judgement is made about the impacts people describe or management strategies they may have tried.

To explore a phenomenon - the experience of living with PDN - a number of research methods are possible, most commonly the use of one-to-one interviews or focus groups (Taylor and Francis, 2013). The research questions in this study seek to understand the personal experience and viewpoint of each participant. The epistemological position of this research accepts the participant experience can be made meaningful by spoken words, and the researcher will interpret these words with sufficient accuracy to reflect the participant's experience (Darlaston-Jones, 2007). If the research questions were seeking reasons for the impact, or a group consensus of perspectives on physical activity and psychological coping, focus groups could have been used. Focus groups can be used to understand why certain viewpoints and perspectives are held by participants (Bryman, 2012). The process of group discussion can give insight to the elements of agreement and/or disagreement about a topic, allowing the researcher insight into the differing perspectives held. Focus groups can be a method for reaching consensus on a topic, but a limitation in this context is that strong personalities can dominate. Less forthcoming personalities may acquiesce to the consensus without agreement (Bryman, 2012).

Other forms of non-verbal communication, such as photographs or artwork have been used to explore the meaning and experience of pain. Studies have used photo essays with adults who had persistent pain to document their experiences of living with pain (Baker and Wang, 2006), or in-depth interviews exploring how the engagement in art supports well-being, despite persistent pain (Reynolds and Prior, 2003). These methods did not fit the pragmatic nature of the research questions. For these reasons one-to-one interviews were considered the most appropriate data collection method (Kvale, 1996; Doody and Noonan, 2013).

*3.4.3 Clinician study – Ontology*

This study asked clinicians about their management of PDN and their perspectives on PMP strategies based upon routine clinical practice. Medical decisions are often effected by subtle nuances of clinical presentation, making no two patients the same (Butler, 2000; Croskerry, 2000).

Although the drive is towards evidence-based health care, specific clinical guidelines do not exist for the patient who presents with a range of health co-morbidities (Greenhalgh, Howick and Maskrey, 2014). Indeed, for patients who have multiple concurrent co-morbidities, clinical guidelines can actively contradict one another. A further consideration is that evidence-based medicine puts empirical studies as the highest level of evidence. There is a challenge to interpreting population data in relation to the single case study patient who sits in front of a clinician (Anjum, Kerry and Mumford, 2015; Eriksen *et al.*, 2013). This leaves clinicians to act as much as artists as scientists, needing to make decisions based on interpretation of the patient narrative and their intuition, as well as objective medical data (Buckingham and Adams, 2000; Greenhalgh, 2002; Edwards *et al.*, 2004). An Interpretivist ontological paradigm was appropriate for this study also.

#### *3.4.3 Clinician study – Epistemology*

The perspective of a clinician is unique, developed through life experiences, professional training, and clinical experience. This study aimed to explore the perspectives of a range of clinicians on PDN management using a social constructionist epistemological position. It did not set out to confirm whether PMP strategies were, or were not, appropriate. A focus group method was felt to be problematic for a number of reasons; firstly, opinions from a range of professionals were required and perceived medical hierarchy may inhibit participants from giving their true perspectives. Secondly, the perspective of primary care practice nurses would likely differ from secondary care medical consultants and so consensus of opinion, which was not the aim of the study, would also be unlikely. Similarly, the perspective of the diabetes multidisciplinary team would likely differ from the pain management multidisciplinary team. Lastly, potential participants were likely to have work commitments across multiple sites and work diaries that would make the practicalities of scheduling a focus group challenging. For an exploratory study, one-to-one interviews were felt the most suitable method by which to discuss these issues with clinicians because it would allow them to give their individual perspective and opinion in confidence.

### *3.5 Selection and recruitment of participants*

#### *3.5.1 Issues of sample size*

There is debate in the research literature about specification of appropriate sample size within Interpretivist research studies (Higginbottom, 2004; Marshall, 1996; Sandelowski, 2000a). Sample size is critical in post-positivist research because statistical calculations depend on sufficient sample population to account for variety within other variables. Qualitative

Interpretivist studies are based within an exploratory context and are not driven by any predetermined hypothesis.

When all the variables that can impact on pain are considered including ethnicity, culture, age and social factors, it would be improbable to recruit a sample that reflected the range of potential variables and experience (Baker and Edwards, 2012). However, a claim may be made to support the results of a study if *data saturation* can be demonstrated. Saturation has been defined as "when no new information or themes are observed in the data" (Mack *et al.*, 2005; Guest, 2006). It has been further suggested that good practice is to specify an initial sample size and then further specify how many further interviews will be conducted, without new themes emerging (stopping criterion) (Francis *et al.*, 2010). Other authors contend that this description of sample adequacy can be taken to mean simply counting thematic codes. This empirical approach to qualitative data is potentially at odds with the philosophical position of these research studies (Morse, 1995). Cutcliffe and McKenna (2002) suggest a claim for sufficient data acquisition should be based on the richness and depth of the data analysis produced.

For both interview studies, no statement of target sample size was made. Rather it was hoped to recruit patient participants who would represent a spread of clinical severity and a breadth of social and cultural backgrounds. It was necessary to exclude potential participants who did not have a suitable level of conversational English. This will be further discussed in *Inclusion and exclusion criteria,* below.

For the clinician study, it was planned to recruit two representatives of the main professions involved in managing pain and diabetes. The choice of two participants could be considered arbitrary as there is no reason why two members from a profession should give a representative voice on pain management strategies. A minimum of two clinicians was however considered feasible and pragmatic.

### *3.5.2 Patient study*

#### *3.5.2.1 Sample population*

This study required people with a confirmed diagnosis of PDN. The study was exploratory; thus, specification of sample size was not set. Rather, it was hoped to achieve a wide range of views on PDN by recruiting a variety of age, sex, ethnicity and duration of diabetes and PDN.

#### *3.5.2.2 Inclusion and exclusion criteria*

The participants were required to have painful neuropathy secondary to diabetes (Coyne, 1997; Higginbottom, 2004), and be able to communicate in conversational English. In order to

limit issues with translation of meaning between languages in spoken conversations, it was felt appropriate to limit participants to those who could engage in conversation without the need of an interpreter (Temple and Young, 2004). This does mean the results and conclusions of this study may not apply to non-English speakers. This decision also implicitly excluded people who communicate by non-verbal means. Sign language translates internal monologue to physical gesture (Temple and Young, 2004), the production of sign language could be considered a further layer of interpretation, even before the interpretation of a translator who would be required to work with the researcher and participant. Such issues are not complete barriers to qualitative research across language divides, but the strategies for dealing with these issues should be transparent. Other exclusion criteria were kept to a minimum - no exclusion was made based on sex, age, ethnicity or type of diabetes – these criteria aimed to allow the maximum variety of PDN experience and management to be reflected by the study participants. Participants were not excluded if they had other persistent pain problems (for example, LBP) but it was made clear that the interview related to impacts that they associated with the PDN they experienced, rather than other pain problems.

*3.5.2.3 Recruitment process*

There were two strategies for recruitment, locally through NHS diabetes and PDN specialist clinics, and nationwide by advertisement in Balance, the peer-support magazine of DUK.

For the local NHS clinics, patients who had a confirmed diagnosis of PDN were given a study participant information sheet (PIS) by their clinician in clinic, see Appendix 3. The PIS included the study aims, the mind-map of strategies used in PMPs and the diabetes complication questionnaire. The mind-map and diabetes complication document are further detailed in Section 3.6. If they had further questions or were interested in being involved, the PIS had contact details for the researcher. On contacting the researcher, further questions about the study were answered and eligibility confirmed. A face-to-face or telephone interview was subsequently scheduled for a mutually convenient date and time.

DUK supported this study with an advert in Balance magazine, which had a national distribution in the UK of approximately 146,000 people with diabetes or family members. DUK membership has an equal sex balance (50% female, 47% male, 3% unknown), is nationwide and representative of the UK population geographically (membership 3% Northern Ireland, 5% Wales, 7% Scotland, and 85% England) and represents all age groups (31% <60 years, 44% 60-79 years, 17% >80 years, 15% unknown). DUK do not have membership ethnicity data, however they do have a stated policy to actively engage ethnic minorities in diabetes awareness programmes that include research studies (DUK, 2015). The advert included brief study information, as well as an e-

mail address and telephone contact details for the researcher. People who contacted the researcher and fulfilled the eligibility criteria were sent the PIS pack for further information on the study. If they were subsequently interested in participating, they contacted the researcher and a mutually convenient date and time was scheduled for an interview.

### *3.5.3 Clinician study*

#### *3.5.3.1 Sample population*

The sample population was staff involved in the medical care of patients with diabetes and PDN, and staff involved in PMPs. Management of diabetes and pain differs between primary and secondary care, so appropriate representation from all areas was sought.

As with the patient study, there were also communication issues to consider with the clinician study. Medical language has evolved to be specific and unambiguous. Diagnostic labels convey much information between HCPs who can assume a large volume of innate information from a short piece of medical terminology. These specific meanings should facilitate quick and accurate communication between clinicians. As a physiotherapist with experience of working with consultant anaesthetists and psychologists, as well as other physiotherapists, the researcher could be considered to have *insider status* with regard to the interview participants (Petty, Thomson and Stew, 2012a; Mack *et al.*, 2005; Finlay, 2002a). Insider status implies a different dynamic of power and status than existed within patient interviews. Shared terminology may facilitate more rapid communication, but could also hide specific meanings if subconscious acceptance of these terms was not considered. A non-clinical researcher would need to ask further questions to clarify meaning of unfamiliar terminology that, whilst increasing the duration of the interview, would ensure the full implication of the clinicians' perspectives were recorded. When forced to slow down and consider the words used, it is not unusual to find that the topic has to be considered more carefully than when using terminology.

The researcher is an active clinician, so it is prudent to reflect on the potential for some aspects of the clinician interviews to have elements of assumption and prejudice from the outset. These limitations will be considered in greater detail in Chapter 4.2.

#### *3.5.3.2 Inclusion and exclusion criteria*

The sample was purposive, with the aim to include at least two members of the main professions involved in managing diabetes and/or pain: diabetes medical clinicians, pain clinicians, DSNs, practice nurses, psychologists, physiotherapists, podiatrists and GPs. Having no clinical role in either diabetes or pain management was the only exclusion criterion.

*3.5.3.3 Recruitment process*

In order to recruit the variety of staff required, clinicians from two secondary care and one primary care NHS organisation were approached to participate. Clinicians in secondary care were identified directly from diabetes and pain services Internet pages and emailed a PIS by the researcher (Appendix 4). As with the patient study, this included the mind-map of pain coping strategies (Appendix 6). Clinicians were required to contact the researcher if they wanted further information about the study. If they were eligible and able to participate a mutually convenient appointment time was arranged to conduct a face-to-face interview.

In order to recruit from primary care, where clinicians do not usually have a clinical speciality, recruitment was via the Primary Care Research Network. The Primary Care Research Network send regular updates of active research projects to all primary care clinicians, this allowed clinicians with an interest in the study to contact the researcher for further information. As with recruitment of secondary care clinicians, if they met the eligibility criteria and were able to participate, a face-to-face interview appointment was scheduled.

*3.6 Materials included with the PIS*

*3.6.1 Patient study*

The PIS can be found in full in Appendix 3. People with diabetes can develop a wide range of potential complications all stemming from the abnormal levels of hyperglycaemia. Microvascular complications include PDN, retinopathy and autonomic neuropathy (Tooke, 1995; Holt and Hanley, 2012a). Macrovascular complications include nephropathy, cardiovascular disease and peripheral arterial disease including ulceration due to poor healing (Donahue and Orchard, 1992; Holt and Hanley, 2012a). People with diabetes can experience greater levels of depression and anxiety than the population without a chronic condition (Biessels, Deary and Ryan, 2008; Bair *et al.*, 2010). Managing diabetes and its complications is known to be challenging (Hinder and Greenhalgh, 2012). Please refer back to Chapter 1 for more details on complications related to DM. PDN is only one of these potential complications and the patient study sought to understand the wider medical complications that interview participants were experiencing, and how much these complications interfered with their lives.

Potential participants were sent a study questionnaire that had sixteen common complications arranged in no specific order (Appendix 5). The layout aimed to give no precedence to any specific complication. It had free space to add any additional complication associated with diabetes the participant experienced. Participants were asked to rank the complications they experienced on a scale as follows: 1=most interfering problem, 2=next most interfering problem,

and so on. Participants were asked to complete this questionnaire once they had agreed to the interview. It was collected in person for face-to-face interviews, or completed verbally for telephone interviews.

#### *3.6.2 Patient and clinician studies*

Participants in both interview studies were asked how relevant they felt strategies taught by PMPs might be to PDN. It could not be assumed however, that either patient or clinician participants would be familiar with the strategies that are taught within PMPs.

To address this issue a mind-map was produced based on British Pain Society guidance and other high quality sources of evidence (BPS, 2013; Geneen *et al.*, 2014; Karjalainen *et al.*, 2009; Williams, Eccleston and Morley, 2012), see Appendix 6 – Pain management programme mind-map. The programme manuals of two secondary care PMPs (Yeovil District Hospitals NHS Foundation Trust and Calderdale and Huddersfield NHS Foundation Trust) were consulted to ensure that active clinical programmes reflected the guidance and were not using any other strategies.

Participants in both the patient and clinician studies received this mind-map. The mind-map outlined the strategies that comprise a PMP, arranged in a circle so as not to imply any one strategy was superordinate to another. There were no descriptions of what these strategies were in practice, but it provided a basis for discussion about how appropriate these strategies appeared to participants for the management of PDN. The mind-map also incorporated a "??" box, this allowed the insertion and discussion of any potentially useful management strategies from the participant's experience. The researcher carried out the interviews and was conscious of the manner in which the strategies were described would not bias participants or suggest particular benefits.

### *3.7 Method for data collection*

#### *3.7.1 Patient study*

An interview method was considered appropriate, as opposed to a focus group, to allow participants to describe the impact of PDN in their own words. An interview would allow them to describe any form of management strategies they had tried and would allow them to give their perspective on PMP strategies in confidence. Interviews can be conducted in a structured format, where a series of questions is followed in the same order for each participant, through to an un-structured format where the interview is completely free flowing, with no specific questions to cover. For these research questions, a semi-structured interview was planned using a topic guide

to ensure all key topics were covered. The development of this guide is covered in section 3.9 Interview content and approach.

Participants were interviewed either face-to-face interview on University of the West of England (UWE) premises or at their own home. The University 'Safety for social researchers' guidance on lone working was followed for interviews conducted at the participant's home. Or interviews were conducted over the telephone as they preferred or locality dictated. This decision was pragmatic, but potential differences between face-to-face and telephone interviews should be considered. Face-to-face meetings are more personal and rapport can be developed more readily. Telephone interviews, however, can allow the participant to be more open with their answers and perhaps more confident to talk about contentious issues, which they may not be in a face-to-face interview (Novick, 2008). There are differences in non-verbal communication and cues between face-to-face and telephone interviews. In interviews conducted away from the participant's home (on University premises or by telephone), the interviewer has no knowledge of the home and local environment in which the interviewee lives. During telephone interviews there are no clues to the interviewee's apparent fitness, body mass index or other cues about personal life – information that has been described as 'ethnographic' (Holt, 2010). Similarly, the interviewee also had no knowledge of the interviewer, other than tone of voice, which may provide cues to social grouping. Existing research that required widening recruitment for similar pragmatic reasons found no differences in data quality between the different modes of contact for interviews (Sturges and Hanrahan, 2004).

#### *3.7.2 Clinician study*

All interviews for this study were conducted face-to-face at the place of work for each participant. This option presented least disturbance to their work pattern. Similar to the patient study an interview guide was used to ensure no key topics were omitted from the interview, please see section 3.9 Interview content and approach, for the development of this topic guide.

### *3.8 Process for informed consent*

#### *3.8.1 Patient study*

In order to provide informed consent, potential participants must understand the possible risks and benefits of taking part in a study (Orb, Eisenhauer and Wynaden, 2001; Department of Health, 2005). Participants had the opportunity to ask questions when initially contacting the researcher and a further opportunity was provided prior to the start of the scheduled interview. The aims of the study, the process of making recordings anonymous, their right to withdraw at any point and the background of the interviewer as a clinical physiotherapist were reiterated prior

to commencing the interview. If participants were happy to proceed with the interview, informed consent was taken. For face-to-face interviews, participants signed a consent form, and for telephone interviews they were asked to make an affirmative statement of consent as the first section of the recorded interview (Appendix 7).

*3.8.2 Clinician study*

Prior to commencing the interview the aims of the study, the process of making recordings anonymous, the participant's right to withdraw at any point and the background of the interviewer as a clinical physiotherapist were reiterated. If participants were happy to proceed with the interview, then informed consent was taken and participants signed a consent form.

*3.9 Interview content and approach*

*3.9.1 Patient study*

Once informed consent was obtained, the initial section of the interview covered demographic questions: age, ethnicity, type of diabetes, duration of diabetes and PDN, any current analgesia and current work status. The demographic data form can be found in Appendix 8.

The interviews were semi-structured based on an interview schedule, please see Appendix 9 for the root questions. This schedule was developed to ensure that the main areas of interest (PDN impact, participant management and participants' views on both physical activity and psychological coping) were covered by the interview. These root questions and potential follow up questions were based upon the existing literature, the research questions and the experience of the research student and supervisory team. They were also discussed with an Expert Patient Research Partner (EPRP), to ensure the questions made sense and were appropriately worded. The participant discourse led the exact order of the interview topics, but the schedule ensured no key topics were omitted.

There was the potential risk that talking about the experience and impact of PDN, could distress participants. There were arrangements in place for Professor Candy McCabe to call any participant who became distressed, with their agreement, to discuss the issues raised, and plan any appropriate intervention. Professor McCabe was Director of Studies for the researcher and has extensive clinical and research experience with persistent pain states (Rheumatoid arthritis, Complex Regional Pain Syndrome, Breast radiotherapy injuries). Some of these clinical services are national centres and one aspect of her role is arranging for appropriate clinical services to be provided near the person's home. This experience of advocacy would be useful were interview participants to have become distressed.

*3.9.2 Clinician study*

The initial structured section of the interview gathered the participant's profession, their experience and role in managing diabetes and PDN, or their involvement in delivering PMPs. The subsequent semi-structured section was guided by an interview schedule developed from the existing literature on PMPs and PDN, and the clinical experience of the researcher and supervisory team (please see Appendix 9b). The interview explored the options participants considered for helping people with PDN manage this condition. It then explored the clinicians' views of physical activity and psychological coping strategies for managing PDN. Finally, it asked about any practical issues that should be considered for potential PDN management interventions.

*3.10 Data preparation – patient and clinician studies*

An MP3 device was used to digitally record all interviews to electronic media. In face-to-face interviews an external microphone was placed between the interviewer and participant, and in telephone interviews the MP3 recorder was connected to the phone line by an adaptor.

Once the interview was concluded, the MP3 files were transferred for secure storage to password protected UWE servers and the original MP3 files deleted from the device. The researcher transcribed the first four patient interviews to Microsoft Word (Microsoft Corporation, USA), and all other interviews were transcribed by a professional secretarial service (Essential Secretaries). The MP3 file was uploaded by secure file transfer and returned as a Microsoft Word document. These documents were then stored on UWE secure servers. The Word documents were anonymised by replacing the participant's name with a pseudonym. Any other identifying details, such as specific UK locations, place names, NHS Trust names, or clinicians were also removed (for example, "I was treated at [NHS Trust]…"). The transcripts were imported to NVivo v10 (QSR International, Doncaster, Australia) for data management and subsequent analysis. The original MP3 files, the transcribed interview documents and the NVivo files were all stored on secure UWE servers. University policies on data management were adhered to throughout these studies.

*3.11 Interview data analysis*

There are numerous methods by which qualitative data can be analysed, depending on the philosophical perspective of the research project and the research questions (Pope and Mays, 2006). Authors have highlighted that reporting the philosophical assumptions present in the analytical process of qualitative research, often lack clarity and explicit detail (Caelli, Ray and Mill, 2008; Braun and Clarke, 2006; Sandelowski and Barroso, 2002). Caelli, Ray and Mill (2008) suggest four key areas that research reports should make explicit: 1) theoretical position of the

researcher, 2) congruence between methodology and methods, 3) strategies for demonstrating rigour and 4) the 'analytic lens' through which the analysis is carried out. Congruence between methodology and methods, and the analytic lens are the focus of the following section. Strategies for research rigour have been considered in the introductory section 3.1.1, and are described in detail throughout this chapter.

There were a number of analytic frameworks that needed consideration, and the analysis should match the research questions as well as the methods employed to gather data.

*3.11.1 Patient study*

The research questions explored the participants' experiences of PDN. Communication of experiences can take many forms, but the most common is spoken word. Analysis of the spoken word can be at the *semantic* level – the words are taken at their face value meaning, or at a *latent* level – where attention is paid to the mode and manner of their delivery (Pope and Mays, 2006; Braun and Clarke, 2013b).

To explore the experiences of PDN management and potential utility of PMP strategies, it was necessary to look for patterns across the data set (all interviews). The eventual results and conclusions needed to reflect the sample population with PDN, not the individuals who contributed to the data. An analytic framework such as Interpretive Phenomenological Analysis (IPA) is focussed on the personal experience of a phenomenon in detail, and so results only claim to be true from the perspective of those few individuals interviewed (de Witt and Ploeg, 2006). IPA has been used in high quality research into peoples' experiences of pain. For instance, Reynolds and Prior (2003) used IPA to examine in detail how people used artistic means to maximise their sense of wellbeing. The results outline the wide range of benefits described by the participants, but these cannot be generalised to all people with persistent pain. IPA has also been used to explore the impact of persistent pain (Smith and Osborn, 2007). In-depth interviews with six participants were analysed using IPA; the results highlighted the negative impact persistent pain had on self-identity, and the further impact that context of social and public engagement had on self-image. These results are reported in detail for each theme with supporting quotes from the participants. Clinicians who read this research could become more attentive to the psychosocial impact of pain on the lives of patients they work with, but this research was not designed to identify therapeutic treatment options.

Thematic Analysis (TA) is considered a philosophically flexible approach which allows it to be used in a diverse range of qualitative studies. Braun and Clarke (2014) make a distinction between "Big Q Qualitative" research which is ontologically coherent with an Interpretivist

perspective, and "Small q qualitative" research which is coherent with a post-positivist perspective (Braun and Clarke, 2014). To say this in another way - Qualitative research could use TA to explore the themes that relate to the experience of living with PDN; and qualitative research could use TA to count the occurrence of themes and link frequency to relative importance. This second approach is consistent with post-positivism as it implies that the 'truth' about PDN impacts can be deduced from the frequency counts of the codes.

Another common analytic approach to qualitative data is Grounded Theory (Petty, Thomson and Stew, 2012b), which aims to develop new theories of social processes. Grounded theory starts with no *a priori* hypotheses or models to fit data to, rather it focuses solely on data gathered from participants who have had experience of the phenomenon in question. From being grounded in this data, new theories of the social process in question can be built. The research questions asked in this study did not aim to define theories for why participants experienced the impact from PDN that they described, or to define theories as to whether or not strategies from PMP were deemed acceptable. There are comprehensive existing theories that consider the multitude of variables affecting the likelihood of pain, as well as clearly identifying that the experience of pain is not only subjective, but has psychological and social ramifications (Engel, 1978; Melzack, 2001, 2005). There were no reasons to suppose that the presentation of PDN would not fit with these existing models.

To summarise at this point, and address the issue of congruence from research questions to methods (Holloway and Todres, 2003; Darlaston-Jones, 2007; Caelli, Ray and Mill, 2008); this research study asked questions of personal experience and perspective (Interpretivist ontology), these topics were spoken about either face-to-face or over a telephone (interview methods within a social constructionist epistemology), and other ethnographic information did not form part of the analysis. The results and conclusions drawn from the acquired data needed to be representative of the population interviewed, although not necessarily generalizable beyond that sample, rather than focussed at the individual level (interview method). The most appropriate analytic framework to use was therefore TA (Braun and Clarke, 2006; Braun and Clarke, 2012).

TA could be conducted with initial theories about what kinds of themes may be produced from the data – a deductive approach. The data could have been sifted and the participants' impacts located within the biological, psychological and social domains of the biopsychosocial model (Engel, 1978). An alternative approach, and that taken, was to use an inductive approach, where no assumptions are made prior to the interview process. The interview process could be considered a blank slate upon which participants were able to freely discuss their experiences of PDN, their strategies for managing PDN and their views of pain management strategies.

The philosophical flexibility of TA has been one of its main criticisms; that is, lacking allegiance to any specified philosophy degrades the approach to one of a generic coding technique, rather than an approach in its own right (Holloway and Todres, 2003; Holloway and Todres, 2007). This is challenged by Braun and Clarke (2014), as well as other researchers in the wider debate around transparency in the reporting of qualitative research (Yardley, 2000; Rolfe, 2006; Caelli, Ray and Mill, 2008; Braun and Clarke, 2013b). The collected responses of these authors are that there must be clarity and transparency in the reporting of why critical decisions are made in designing a research study.

Having described the ontological and epistemological positions within this research, the 'analytical lens' used to survey the data needs to be explained. This needs to come full circle to address the research questions, otherwise qualitative research risks becoming focussed on methodology rather than research product (Sandelowski, 2000b). By exploring the experiences of people with PDN and their perspective on the utility of PMP strategies, the analysis needed to be equally pragmatic (Feilzer, 2010; Smith, Bekker and Cheater, 2011). In practice this meant there were two possible extremes when analysing the results – at one extreme all participants would value all PMP strategies and feel they are totally suitable to their experience of PDN. The other extreme was that all participants would fully reject the suitability of all PMP strategies for helping them to manage PDN. The reality was likely to be somewhere between these extremes and it would be for the researcher to consider how to use the resulting analyses, by considering: were there any indications of potential pragmatic practical treatment options for people with PDN present in the analysis?

These considerations were important for the current studies and when considering potential future research. For instance, if there were mixed participant perspectives on a certain pain management strategy, criteria would be required to include or exclude it from a possible PDN intervention.

### *3.11.2 Clinician study*

Much of the justification for using TA within the patient study was also applicable to the clinician study. It could not be taken for granted that all clinicians interviewed would have a thorough understanding of the strategies taught within PMPs. Since nothing was known about the clinicians' perspectives, there was the potential for positive, negative and ambivalent viewpoints on PMP strategies. This exploration suited an inductive TA approach, as no assumptions were made regarding the perspectives clinicians might hold.

There were some differences in the research questions between the patient and clinician study. The clinician study was not asking about the clinicians' experience of pain, but rather their professional perspectives on the management of PDN and the potential utility of PMP strategies. There was no phenomenon to be explored. There were still internal clinical reasoning processes and pragmatic perspectives on PMP strategies that were best explored through a spoken conversation.

*3.11.3 The process of analysis*

There are seven stages to TA; 1) transcription of interview data; 2) repeat reading and familiarization with the dataset; 3) complete coding across the dataset; 4) searching for themes; 5) reviewing the themes produced; 6) defining and naming themes; and 7) writing the dissemination report (Braun and Clarke, 2013a).

Recruitment and interviews for the two interview studies took place concurrently. The early processes for coding and identification of themes also occurred concurrently. The supervisory team identified issues with both coding and theme production by the quality assurance processes that were in place. These issues would have led to researcher bias in the results. The steps taken to mitigate this potential bias are described.

*1) Interview transcription*

The researcher transcribed the first four patient interviews verbatim. This allowed an immersion in these interview texts and led to an appreciation of how dis-jointed both interviewer questions and interviewee answers can be when transcribed. Due to the significant time commitment required, later patient interviews and all clinician interviews were transcribed by professional secretarial services. When transcripts were returned in Word format, they were read alongside the audio MP3 file, to check for accuracy. Secretarial services used a system of highlights where unfamiliar words had been spelt phonetically, where participant and interviewer spoke over one another, or where sections were inaudible (MacLean, Meyer and Estable, 2004). By re-reading and re-listening to the interview recordings, the transcripts could be edited to produce an accurate reflection of the discourse.

There are academic discussions over the merit and necessity of verbatim transcription (Halcomb and Davidson, 2006; Davidson, 2009). The arguments centre on the difficulty of turning spoken word, with all the nuances of intonation and inflection, to written text. This research was not using an in-depth linguistic analysis such as conversation analysis, where it is necessary to code each utterance and pause in the transcription (Irvine, Drew and Sainsbury, 2012). While these research studies do not require a complex notation system to code such pauses, they do

require verbatim transcription because these words are the only mode by which the participants were asked to convey their experiences of PDN. These interviews were required to be as faithful as possible, as they formed the data on which analysis was based.

Along with the transcribed verbatim interviews, two forms of supplementary notes were kept. Most interviews were reflected on for their conduct and process. These field notes contained initial thoughts or unexpected topics that had arisen in the interview and reflections on the conduct of the interview. A reflexive diary was also kept using Evernote, a cloud based note storage application that can be updated from laptop, desk PC or smart phone. This diary was used to keep a record of important conversations, emails with supervisors, and insights that occurred. The data from field notes and the reflexive diary were not part of the data set used for the analysis. They were used as part of the quality management process that will be described in the subsequent sections on the process of analysis.

These multiple processes: recording notes on conduct of the interviews, maintaining a reflexive diary and the actual transcribed data from the interview, provide a triangulation of sources that can be returned to in the next phase of analysis. This triangulation allows the researcher to revisit the context of the interview in audio, as well as typed form, to check the meaning has not been misunderstood (Halcomb and Davidson, 2006). These processes were appropriate to the needs of the research methodology and research questions being asked.

*2) Familiarisation with the data*

Historically, becoming familiar or immersed with qualitative data required hardcopy printouts of interview transcripts. These were read repeatedly and important sections, at least in the opinion of the researcher, were highlighted. These approaches encouraged physical immersion with the data, but were not amenable to quick cross-referencing large volumes of data or finding participant quotes.

Computer Assisted Qualitative Data Analysis Software (CAQDAS) packages have been developed and refined over the past 20 years (Johnson, Dunlap and Benoit, 2010). Prior to starting the analysis, the researcher attended a two-day NVivo training course. A key message was that such software provides a platform for the analysis by storing and managing the data – it does not perform the analysis (Johnson, Dunlap and Benoit, 2010; Johnston, 2006). Further, the use of computer-assisted strategies does not guarantee that research produced would be of greater quality than research using manual strategies (Paulus *et al.*, 2015). The use of NVivo has potential risks and benefits that must be understood by the researcher, preferably, prior to investing significant time in becoming familiar with the software.

A risk for this research was that NVivo software features, such as searches for particular words and their resulting frequency counts, might be confused with relative importance in later analysis. The topics that participants were likely to discuss could have a plethora of synonyms. For instance, a search for "Pain" across all interviews would not capture the participants describing their symptoms as throbbing, aching, or nagging. A search for "my sleep is disturbed" would miss reference made by participants to "my sleep is rubbish" or "I hardly get any sleep at all". Paulus *et al.* (2015) describe these analytical approaches as *software-driven*, where software technical capabilities have excess influence on the conduct of the analysis. The use of such CAQDAS features is not wrong *per se,* but would not be complementary to the philosophical position of these research studies. The analysis of these research studies had to be built from the interview data the participants had given and software techniques would not facilitate that process.

This researcher used NVivo (v10, QSR International) at a basic level. NVivo allowed interview transcripts to be stored as *sources*, and then accessed for coding. NVivo allowed *nodes* to be created; these nodes were a collection of references extracted from the interview sources that related to a specific topic contained in the interviews. This use of CAQDAS was *method-drive*, where the functions of the software were subservient to the analytical approach being used (Paulus *et al.*, 2015). As new topics were raised in the interview, new nodes were created as required. For clarity, and for consistency with the approach of thematic analysis, the term *code* will be used from here, in place of *node*. These basic functions and the ability to access the dataset from multiple work places, were felt to outweigh any philosophical or tangible distance from the data that CAQDAS software may create (Bringer, Johnston and Brackenridge, 2004; Hutchison, Johnston and Breckon, 2010). The specific use of NVivo through the analysis will be described in each following section for transparency (Paulus *et al.*, 2015; Woods *et al.*, 2016).

The anonymised Word transcripts were imported to NVivo for re-reading and later analysis. The transcripts were read a number of times to embed the conversations, and the main topics and issues discussed.

*3) Complete coding across the dataset*

The data within each individual interview were coded; this means small units of text were highlighted and assigned codes that captured the essence of what had been stated by the participant. New codes were created as required by the data.

A code has been described metaphorically as a brick in a wall, or as a piece of fabric in a patchwork (Braun and Clarke, 2013b). It is the smallest unit of data; each code should contain reference to only one specific topic. The data were coded to include the surrounding text that

provided contextual background. In the example below (Figure 9) the text included as 'Effect on family', also included text that became coded as 'Delays in treatment'. The language was impossible to separate without losing all sense of what was being spoken about.

The example below uses a pseudonym to provide anonymity to the participant, and has removed a self-reference to their given name.

Figure 9 - Example of interview coding.

*INTERVIEWER:*

*you mentioned three obvious areas of impact the pain itself and how it impacts on your mobility on your sleep and you said it was bringing you down*

*MARY:*

*Yes, so emotionally it was just like, so I suppose, I just got very depressed I think even to people I was still smiley [personal name]. I knew I had stopped really eating properly, you almost give up because nobody else is like taking notice at home. My husband and both my sons everybody could see that it was making me ill just purely because I wasn't getting the answers that I wanted, and the treatment I wanted it was making me ill as well as sort of…*

*Coded as:*
*Emotional depression*
*Nobody is listening*
*Effect on family*
*Delays in treatment*
*Can't face food*

The analytic process cycles between the codes and the data, creating new codes as required. Often an existing code would be close to the issue of the new text requiring coding, but not sufficiently close to allow the existing code to be used. In these cases a new, precise code was created to maintain an accuracy and richness to the data (Lambert and Loiselle, 2008). Richness of data refers to deeper, rather than superficial, engagement with the interview text. To engage in superficial coding requires a level of interpretation on the part of the researcher, moving from interview text to code. Such superficial coding maybe appropriate for some research studies, but this study was exploratory and there was uncertainty regarding the issues that would be raised. If

researcher interpretation is allowed too early in the process it risks introducing bias to all future layers of analysis (Pope, Ziebland and Mays, 2000).

*3.11.4 Process orientated quality assurance – coding the data*

The supervisory team have extensive experience of qualitative research and were instrumental in developing the research student's understanding and conduct of the research studies by a rigorous review process and both verbal and written feedback.

The researcher's experience as a clinician includes training in motivational interview and empathic listening skills. It became clear that while useful in the clinical interview, some of these skills became leading questions in a research interview. The reflective listening skill of summarizing a section of clinical interview, for instance "That situation sounds very distressing", can lead a patient to divulge further information that is useful for developing a clinical management plan. In a research interview this phrase may put the idea of *distress* into the words of the participant.

Interviewers must maintain a neutrality and impartiality or be at risk of introducing researcher bias into the data (Cohen and Crabtree, 2008). To address this issue a series of coached role-play sessions were established with Professor McCabe and an experienced research nurse, this coaching allowed the interview wording to be analysed and immediately critiqued. A key development in the researcher was to accept a topic like sleep quality, although frequently referenced in the PDN literature, might not be raised by the interviewee. If this topic were not raised, it would be inappropriate to direct a question towards their experience of sleep, as this leads the interview by the researchers' expectations, not the subjective experience of the participant.

For patient and clinician studies, researcher bias was identified in the early phase of the coding process. The first phase of coding was conducted between October 2013 and September 2014, when coding of early interviews was happening concurrently with recruitment and conduct of later interviews. When the supervisory team reviewed the early codes, it was clear the names of the codes were being created with the research questions in mind. For instance, *PDN impact - mood, PDN impact - sleep and PDN impact - family* suggest that, based on the existing PDN literature, there was an expectation of certain impacts participants would experience. It was not possible to satisfactorily address this issue by re-coding the data within the existing NVivo project, so this project was closed. A new NVivo project was established and all patient and clinician interviews were re-coded between November 2014 and March 2015.

*4) Searching for themes*

Once all interviews within each study had been fully coded, the codes created were grouped together to form higher-order themes. Themes can be considered as having a central organising concept that unites the codes within them (Braun and Clarke, 2013b). Metaphorically, the themes are the patchwork quilt created with pieces of fabric, or the house built with bricks. A theme should be internally consistent and coherent from the codes it contains, and each theme should be exclusive.

Where there are a large number of codes, managing the data on-screen through NVivo becomes difficult. Hard copies of the codes were therefore created then cut up into individual codes and brought together into groups that appeared similar. For example, any code related to sleep could be grouped, whether it related to getting to sleep, staying asleep or sleeping through the day.

The process of drawing themes together allows the consistency of coding to be checked and has been termed 'constant comparison' (Mays and Pope, 2000; Pope, Ziebland and Mays, 2000). NVivo facilitated this process of constant comparison because it allowed immediate access back to the source data. For example, there were two codes that related to 'sleep disturbance' and 'difficulty getting to sleep'. The data within these codes could be checked to establish whether these two codes were appropriate to merge because they have coded the same issue, or whether PDN actually causes two distinct impacts on getting to sleep (sleep initiation) and staying asleep (sleep maintenance). The title of the code could also be checked to ensure that it accurately portrayed the data it contained. This process facilitates the consideration of whether two unique issues about sleep are contained within the dataset, so developing an "analytic richness" (Bringer, Johnston and Brackenridge, 2004).

Although all the interview dataset had been initially coded, the process of returning to the data and the codes produced (constant comparison), refined the codes into unique entities and allowed the produced themes to be constantly refined.

*3.11.5 Process orientated quality assurance – producing themes*

As the codes were analysed to create themes, the supervisory team examined these outputs. The issue of researcher bias, identified earlier, was again identified. The first phase of codes that had been created were used to form themes that were focussed on the research questions. Themes were developed that related to the impact of PDN and participant views of management. These themes were devised with the research question as the primary focus, not the data elicited from the interviews. This was a process of deductive analysis, taking an initial hypothesis or model and examining the data to see whether it can be supported. A deductive

approach is compatible with qualitative research as research from Dures *et al.* (2012) highlight, but it does not sit congruently with the research questions or the philosophic position of these research studies (Holloway and Todres, 2003). The decision had been taken to re-code all data, and hence the first phase of analysis was also stopped. Once the re-coding was complete, the development of themes and super-ordinate themes was re-started, using inductive principles as described.

These quality assurance processes at coding and theme production were circular not linear, as there were overlaps between the phases of data gathering, coding and analysis. These processes were not aimed at ensuring that there were high levels of agreement between researcher and supervisory team, this could be considered an inter-rater reliability score for the analytic process and would be appropriate to research sited in a post-positivist paradigm (Morse *et al.*, 2002). Rather, they were used to ensure that the researcher's approach to the process of data acquisition and analysis was neutral and appropriate for the nature of these studies. These studies were situated in an Interpretivist framework, where the interpretation of the researcher would be slightly different than that of the supervisory team. This remains appropriate because it was the researcher who had the deep and prolonged engagement with the data, rather than the supervisory team.

*5) Reviewing the themes*

The development of a theme structure requires consideration of whether themes naturally coalesce into a higher level of pattern. These superordinate themes should still have a central concept they embody, but they will encompass different facets of that concept within the themes they contain. It is only at this point when the patterns of codes, themes and superordinate themes have been developed, that these patterns can be examined in relation to the research questions asked.

### *3.12 Expert Patient Research Partner involvement*

Exploratory qualitative research has certain pre-judgements inherent from the start, most notably the life experiences and prejudices, both positive and negative, present in the researcher (Finlay, 2002b; Le Gallais, 2008; Johnson, Long and White, 2001). Is it possible for a researcher with no experience of persistent pain or diabetes to know what questions to ask? The involvement of patients in research design and conduct is increasingly recognised as good practice (www.invo.org.uk). The patient perspective on the impact of disease has highlighted that clinician researchers are not necessarily best placed to independently decide the direction of future research (Gooberman-Hill, 2012; Dures *et al.*, 2016; Hewlett *et al.*, 2005).

In order to recruit an EPRP to this project, a recruitment letter was sent to all patients who had been assessed at a specialist tertiary clinic for PDN between 2010 and 2013 (n=53). This aimed to recruit one or two people who had an interest in the research process and felt they could contribute their experience. Only one person responded to this letter. They have played a role in this research in a number of ways. Firstly, by contributing to research design and collaborating in developing the interview schedule for the patient study. The EPRP also helped develop and revise the PIS for the study recruitment and discussed the emerging coding and themes of the analysis with the researcher.

Although the patient experience is becoming more common in health research, it is not universal. Some researchers feel that EPRPs do not bring an un-biased perspective to the research and do not have sufficient academic experience of the research process (Staniszewska *et al.*, 2007). It is therefore important these relationships are managed carefully, appropriate training is provided and the contribution of EPRPs is clearly recognised in the outputs of the research (Brett *et al.*, 2014; Elberse, Caron-Flinterman and Broerse, 2011). The supervisory team all have extensive experience of patient engagement and involvement with other research studies and facilitated training sessions with the EPRP on research methodology.

### *3.13 Interview ethical considerations and approvals*

Health researchers, working with people who have a variety of physical and/or mental health conditions, need to be aware these conditions can make people feel vulnerable and exposed to potential exploitation. Exploitation can occur due to the asymmetric relationship of power between patient/participant and clinician/researcher (Townsend, Cox and Li, 2010). Exploitation can include the participant not understanding they are part of a research study, by giving an intervention against someone's will, by withholding an intervention that is indicated or by using someone's personal experience to produce qualitative research reports without acknowledging their contribution.

Ethical considerations for research involving people as participants, are based on *autonomy*, *beneficence* and *justice* (Orb, Eisenhauer and Wynaden, 2001). The considerations aim to ensure that potential participants understand the nature of the research, actively choose to be part of that research and are dealt with fairly throughout the research process.

During interview research, it is important that the participant can lead the interview discourse. The interviewer should keep the interview schedule in mind, but there is no need for the interview to follow the same order for each participant. Open-ended questions such as "How does painful diabetic neuropathy affect you?" could be used to allow the participant to discuss

the issues they felt had the greatest priority. This approach is the opposite of an interviewer-led structured interview and supports the participant's autonomy. The PIS designed for these studies also aimed specifically to facilitate autonomy.

Beneficence means maximising potential benefits to participants and doing no harm to them (Orb, Eisenhauer and Wynaden, 2001). Being a participant in an interview study has no immediate benefits to the participants, and has the potential to be physically and emotionally distressing. Physical distress might have occurred due to prolonged sitting for the interview. One interview was split into two sessions because the participant needed to take a break. Emotional distress may occur when talking about the range of impacts that PDN has had on their lives. It is also important participants do not feel judged by the interviewer. Having chronic health conditions, which have led to physical health and mental health problems, should not be judged either explicitly or implicitly through the course of the interview (Townsend, Cox and Li, 2010). To manage potential distress in a clinical consultation requires empathic communication skills developed through clinical experience. Arrangements were in place for Professor McCabe to contact participants were they to have become distressed in a manner that could not be managed in the moment.

For participants to have confidence to share personal information, it was vital they could not be identified in any way. Any information that could identify a participant was removed; this included their name by using pseudonyms in the transcription, removal of any specific home locality, NHS or other health organisations and to specific clinicians involved in their care. This last point is important for the clinicians who are involved in the patient participants' care, as participants' views may reflect negatively on the care received by these clinicians. Anonymity was also important for clinician participants to feel confident in talking freely about their clinical practice and approach to the management of PDN.

Personal data from interview participants must be protected. Interview transcripts, quotes used in poster presentations, thesis chapters and academic papers have had all personal information removed. The participant data including full names, addresses and phone numbers, sociodemographic and clinical details were kept in an electronic study spreadsheet. This file was password protected and kept on UWE servers that required further password security measures to access. UWE have data management policies on the storage of electronic patient sensitive data that were adhered to fully throughout the research process. These data will be destroyed after nine years, in accordance with these guidelines.

All participants were made aware that the researcher was also a practicing physiotherapist, experienced in managing persistent pain. This was made explicit in the PIS and in the opening of the interview. It was the opinion of the researcher that it would have been disingenuous to conceal this fact from participants. This decision did however create the dual role of clinician-researcher and the potential for conflict between these roles (Houghton *et al.*, 2010). Patient participants occasionally asked for clinical advice during the process of the interview. It was not the role of the researcher to give advice or to suggest treatment interventions the person had not been given the opportunity to trial. With experience the researcher became more adept at bracketing such questions, and then returning to them at the conclusion of the interview. This allowed the interview to focus on the research topics, but also gave due time to the patients' requests. In answering these questions, it was always stressed that the researcher, despite being a clinician, was not acting in a capacity to alter treatment or suggest other interventions.

*3.13.1 Patient study - Approvals*

Ethical approval for this study was obtained from the UWE Health and Applied Sciences Faculty ethics committee, from the NHS National Research Ethics Committee (Frenchay) (Study identifier 13/SW/0125) and from University Hospitals Bristol NHS Foundation Trust (UHBristol) Research and Innovation department (Study identifier ME/2013/4345). The relevant permissions letters can be found in Appendices 11-13.

In order to widen recruitment a national advert was placed through Balance the DUK membership publication. A substantial amendment was submitted for approval and granted by Frenchay NREC, please see Appendix 13 – REC substantial amendment.

*3.13.2 Clinician study - Approvals*

Ethical approval for this study was obtained from the UWE Health and Applied Sciences Faculty ethics committee. To approach clinicians in secondary care, proportionate review approval was secured from the Research and Innovation departments of University Hospitals Bristol NHS Foundation Trust (Study identifier ME/2013/4340) and North Bristol NHS Trust (Study identifier 3164). To approach clinicians in primary care, a letter of access was secured from Bristol Community Health. The relevant permissions letters can be found in Appendix 14 – Clinician permission letters.

*This chapter has outlined the decisions made in conducting two interview studies. Starting from the research questions it has detailed the philosophical perspectives these studies were located within. It has detailed the methods used to sample and recruit participants to these*

*studies, how the interview topics were formulated and how the interviews were conducted. The analytical process has been clearly described and shown to be congruent to the research questions. Processes for quality assurance of these research studies have been described.*

*The following two chapters will present the results of these studies. Each chapter will contain individual discussion and conclusions.*

# Chapter 4 – Results from the patient interview study

*The preceding chapter outlined the methodological considerations relevant to the planned interview studies. It described the decisions taken to provide a coherent approach from research questions to analytic framework. Chapter 3 also described specific methods that were followed in the conduct of these two studies. The following chapter will present the detailed results and discussions for the study with people who experience PDN. Further reference in this chapter to 'participants' relates only to patients who were interviewed. The results from the interviews with clinicians are presented in Chapter 5.*

## *4.1 Interview participant characteristics*

All potential participants who contacted the researcher having received the study information were interviewed, except one, who did not meet the inclusion criteria as they had neuropathy but no pain. Twenty-three participants were recruited with a mean age of 62 years (range 24-86 years); 12 were women. All except one participant identified themselves as White British. Ten participants had Type 1 diabetes. Participants self-reported being diagnosed with diabetes for a mean of 23 years (range 7-50 years) and having experienced PDN for a mean of 10 years (range 1-24 years). A summary of participant characteristics is presented in Table 8, further interviewee details can be found in Appendix 15. The interviews lasted between 30 and 120 minutes.

Table 8 - Participant characteristics

| **Characteristic** | **N** | **Mean (range)** |
|---|---|---|
| Participants | 23 | |
| Gender | | |
| *Female* | 12 | |
| *Male* | 11 | |
| Age years | | 62.5 (24-86) |
| Ethnicity | | |
| *White British* | 22 | |
| *West Indian* | 1 | |
| Type 1 diabetes | 10 | |
| Type 2 diabetes | 13 | |
| Duration with Diabetes (years) | | 23.5 (7-50) |
| Duration with PDN (years) | | 10.3 (1-24) |

| Characteristic | N | Mean (range) |
|---|---|---|
| Current analgesia | | 2 (0-4) |
| *Anti-epileptics* | 9 | |
| *Amitriptyline* | 8 | |
| *Strong opioids* | 7 | |
| *Paracetamol* | 5 | |
| *Duloxetine* | 3 | |
| *Co-codamol* | 2 | |
| *Capsaicin cream* | 1 | |
| *Nil analgesia* | 5 | |
| Current employment | | |
| *Retired* | 20 | |
| *Full time* | 2 | |
| *Other* | 1 | |

*4.2 Results of participant diabetes complication questionnaire*

To be eligible for this study, participants all experienced PDN as a complication of their diabetes. In addition, they experienced a range of other complications related to their diabetes, please see Chapter 3, section 3.6.1 for details of the complication questionnaire. Table 9 shows the occurrence of complications. Although the study eligibility criteria required participants to have PDN, not all participants scored this complication. This may have been due to the questionnaire lacking clarity whether it was asking about all complications of diabetes, or only those experienced in addition to PDN. In the free text options participants did not identify any further complications they experienced, which were not already part of the questionnaire form.

Table 9 - Participant complications associated with diabetes

| Issues participants associated with diabetes | N | % |
|---|---|---|
| *Painful neuropathy* | 17 | 74 |
| *Glycaemic control issues* | 13 | 56 |
| *Sensory loss* | 11 | 47 |
| *Retinopathy* | 10 | 43 |
| *Mood issues* | 9 | 39 |
| *Weight management* | 8 | 35 |
| *Nephropathy* | 7 | 31 |
| *Sex life* | 7 | 31 |
| *Hypertension* | 7 | 31 |
| *Cardiovascular disease* | 6 | 26 |
| *Bladder issues* | 6 | 26 |
| *Bowel issues* | 6 | 26 |
| *Foot ulcers* | 5 | 22 |
| *Memory loss* | 5 | 22 |
| *Liver disease* | 3 | 16 |
| *Frozen shoulder* | 3 | 16 |

Table 10 Shows how participants considered these complications interfered with their lives. There was variation in how participants completed the questionnaire. Participants did not always rate the complications in a strict sequential order of interference (where 1=greatest interference, to *X* as required).

PDN was the most frequent complication identified (74%). As noted earlier, not all participants rated PDN for the interference it had on their lives. PDN had the highest interference score for impacting on participants' lives (median 1, (interquartile range (IQR) 0)).

Thirty-nine per cent of the cohort identified mood problems as an issue but these moods, when present, were rated the second most interfering aspect of diabetes (2(0)).

The third ranking complications for interference included glycaemic control (3(2)), foot ulceration (3(1)), cardiovascular disease (3(2)) and nephropathy (3(1)). Although these complications have similar ratings for interference, control of blood sugars was endorsed by 56% of the participants, whereas the others were endorsed by 20-30% of the participants.

Table 10 - Participant interference rating for complications

| **Complication** | **Participant count (n)** | **Interference rating (median, (IQR))** |
|---|---|---|
| Painful neuropathy | 17 | 1 (0) |
| Mood issues | 9 | 2 (0) |
| Retinopathy | 10 | 2 (1.5) |
| Sensory loss | 11 | 2 (1.5) |
| Weight management | 8 | 2.5 (1.5) |
| Glycaemic control issues | 13 | 3 (2) |
| Foot ulcers | 5 | 3 (1) |
| Cardiovascular disease | 6 | 3 (2) |
| Nephropathy | 7 | 3 (1) |
| Bowel issues | 6 | 3.5 (1) |
| Liver disease | 3 | 4 (0.5) |
| Hypertension | 7 | 4 (3) |
| Memory loss | 5 | 4 (4) |
| Sex life | 7 | 4 (3) |
| Bladder issues | 6 | 4.5 (3.25) |
| Frozen shoulder | 3 | 5 (1) |
| *Interference rating anchored with 1=most interfering complication of DM* | | |

*4.3 An overview of the thematic structure of patient interviews*

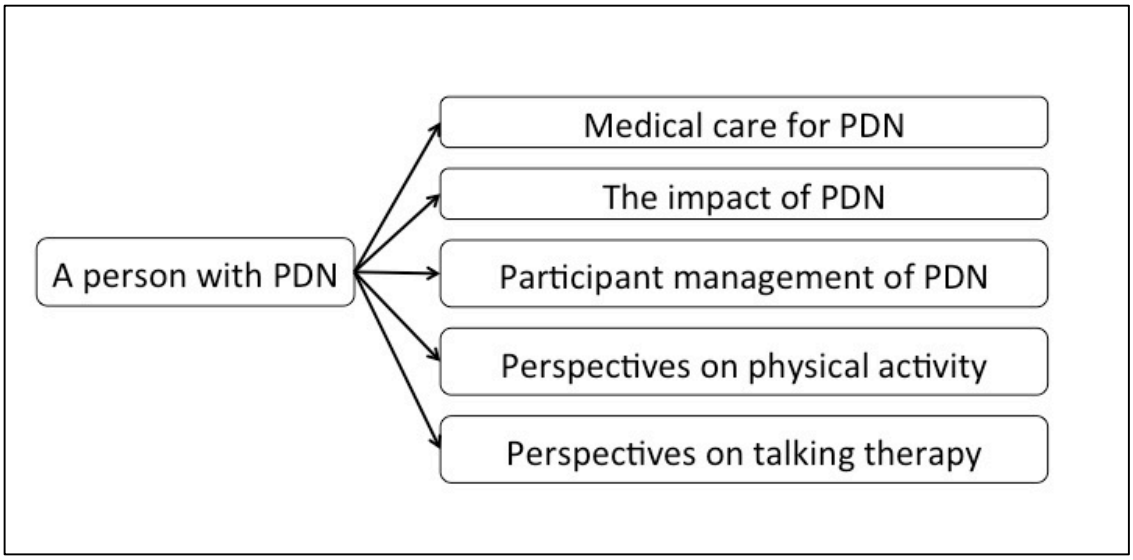
The interview data were coded using the principles of TA (Braun and Clarke, 2012). Each code created referred to a unique issue raised by participants. These codes were grouped into organising themes that contained a central concept. Themes were then further brought together as superordinate themes where appropriate. Full details of this approach can be found in Chapter 3, section 3.11.

The first attempt at interview coding was started once the first three interviews had been conducted and continued concurrently with on-going recruitment and interviews. This first attempt at coding was discarded, (see Chapter 3, sections 3.11.4 and 5) due to potential researcher bias. The second attempt at coding, presented here, was completed when recruitment had stopped and all interviews conducted. The history of code creation showed that no new codes were created beyond interview 13. It would have been unethical to discard interview transcripts simply because the creation of new codes appeared not to be required. Participants had given their time to be interviewed and consented to be involved with the expectation that their contribution would be used. It was appropriate to give due respect to the data that had been provided by all participants interviewed.

Quotes from participants have been used to illustrate codes or themes as required, and these are identified by pseudonym, sex (M/F) and age.

The superordinate themes (Figure 10) were: *Medical care for PDN* - all participants had tried a variety of medication strategies to alleviate pain and subsequent impacts. This superordinate theme provided the context of treatment recommendations participants had received, against which they had explored other strategies to manage their PDN. *The impact of PDN* presented the range of impacts PDN had on participants' lives, these ranged across all manner of day-to-day activities. *Participant management of PDN*, included all non-medication strategies that participants had experienced. Two superordinate themes explored the participants' perspectives on PMP strategies: *Perspectives on physical activity* and *Perspectives on talking therapy.*

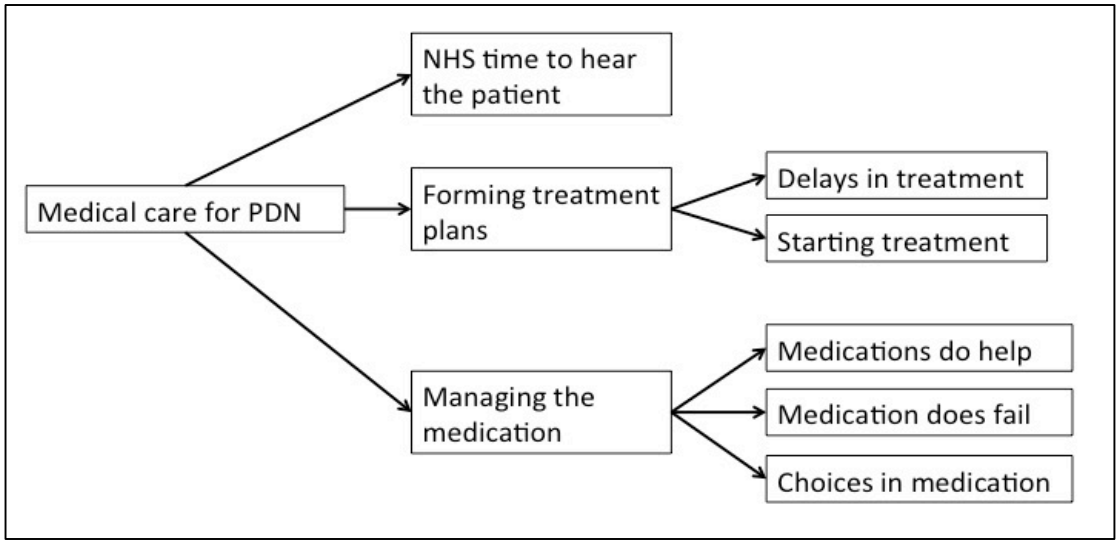
Figure 10 - Superordinate theme overview for patient interviews




*4.4 Superordinate theme: Medical care for PDN*

Before exploring the impacts of PDN described by participants, and the strategies they had developed or experimented with for managing this, it is important to outline their experience of PDN management from the clinical teams they have contact with, both secondary care Consultants and primary care GPs (Figure 11). These issues were not the focus of the thesis, but were important to provide the context within which patients sought to improve their own management of PDN and its' impacts. Participants spoke at length about their journey to PDN diagnosis and how their clinical team currently managed PDN and the associated impacts. This superordinate theme contained three themes - *NHS time to hear the patient, Forming treatment plans* and *Managing the medication*.

Figure 11 - Medical care for PDN - themes and subthemes



*4.4.1 Theme: NHS Time to hear the patient*

Participants had experienced a variety of clinical pathways from their first experience of PDN-like symptoms to diagnosis and treatment. Some participants described their GP identifying the likely pathology almost immediately.

> *"I went to the general GP and said look I've got these burning, burning in my feet and he just said it'll be neuropathy…" Philip, M57.*

Others described many consultations and test procedures over several years before a diagnosis was established and treatment initiated.

> *"I believe the nerve damage that I have got has been caused because I had it for such a long time before my GP referred me to [secondary care specialist]." Joan, F57.*

Participants had a variety of experiences of clinical consultations. Some described being moved through clinic appointments, without feeling involved in the process:

> *"I would say this conveyer belt of you know line up, go in one by one, blood pressure, blood sample, urine sample, go through the motions of it, oh you're overweight yeah, okay I know [laughing] um, and, and our practice is very professional, I get er a printed sheet and goals at the bottom, sometimes I wonder if we've been at the same meeting" Jane, F68.*

When describing their experience of clinical consultations participants described feeling that clinicians had set formats to their consultation that did not often include enquiry about pain.

> *"… you go and the talk is how your kidneys are, how your liver is, how your blood is, how your eyesight is, you know, all these different categories, your blood sugars, your blood pressure, your cholesterol, your fine, goes through the whole, but there doesn't seem to be any, anything automatic for nerve pain." Lisa, F69.*

Closely linked to this issue, was the feeling of not being heard by the clinician, even when they were able to talk about the problems they experienced related to PDN.

> *"so you almost in a way give up and think nobody is listening to me I'll just be quiet I'll just almost shut up." Mary, F44.*

The lack of being heard created a sense their problems were being dismissed or they were in the wrong place to raise them. Other participants however, described their problems were heard and acknowledged, and then some form of treatment was forthcoming.

> *"He said there are tablets out there you know and he was really the first person I thought 'no, he's listened to me', he sounds like he understands how disabling it's become for me" Mary F44.*

> *"The pain management people came up and they were very good, they listened to everything and they prescribed all the tablets." Barbara, F80.*

These descriptions suggest that getting clinicians in the health service to attend to and understand the nature of the persons' problems could present a challenge. Patients described feeling disempowered from raising the key issues they wanted to discuss with clinicians.

*4.4.2 Theme: Forming treatment plans*

This theme contained two subthemes: *Delays in Treatment* and *Starting treatment*. *Delays in Treatment* (4.4.2.1) - participants described the process of reaching some form of treatment for PDN, this journey may have been delayed by clinical inertia or lack of diagnostic certainty. *Starting treatment* (4.4.2.2) - once treatment was started this was usually the prescription of medication, and advice to focus on overall diabetes management.

*4.4.2.1 Subtheme: Delays in treatment*

Participants had experienced delays both in diagnosis or, once the diagnosis was confirmed, delays to starting any form of treatment. For some this was due to seeing different GPs in primary care, which they reported had led to a lack of co-ordinated care planning. For others, they had no real explanation for why these delays occurred.

> *"There was a big period of time between first it occurring and actually getting somebody to deal, properly deal with it." Sam, M53.*

> *"we're talking from seven years from having the symptoms to only about three years ago, so it took a good four years to get to the point where actually some treatment was started and then it took another two years no three years to get to the point of seeing a professor that was interested in diabetic painful neuropathy and being told 'Well actually you still haven't been put on the NICE guidelines of what they say the cocktail of drugs are' as a starting point, so we still hadn't got to that point six years on." Mary, F44.*

*4.4.2.2 Subtheme: Starting treatment*

Participants described the process of reaching and initiating agreed treatment plans with their clinical teams. Some participants described a palpable sense of relief that something was being done. The treatment plans participants experienced were centred on prescription of analgesic medication and close management of blood sugar levels.

> *"Yeah, I think medication came up pretty quickly, and it was, like, the obvious, it was almost like a no-brainer. You've got neuropathy; well, you'd better try some medication." Sally, F48.*

> *"to start to try some drugs to see how we go even if it took for the next two three years messing about with drugs, upping them, but to get on that ladder if you like to start was a big relief to me that we were going to do that." Mary, F44.*

Clinicians encouraged patients to manage their blood sugar levels closely within the recommended parameters.

> *"…it's a matter of keeping your blood sugar levels correct…" Daniel, M67.*

> *"…he [GP] just said to carry on taking the Paracetamol and just see how things went, to keep my blood sugars as tight as possible." Mary, F44.*

However, with different clinicians involved at different times, participants described receiving contradictory advice as to how closely monitored and managed their HbA1c should be.

> *"we're trying to get it between five and eight or five and seven [%HbA1c]. Everybody has a different thing, every Doctor has a different opinion and [one] says 'no I'm quite happy if it's ten, I'm quite happy if it's nine', some will go, 'I'm not happy, it's too high that now and you know we need it at seven'. Do you see what I mean?" Philip, M57.*

*4.4.3 Theme: Managing the medication*

All participants had some experience of medication trials from primary care, secondary care or both. Three subthemes have been constructed from these experiences: *Medications do help* (4.4.3.1), *Medications can fail* (4.4.3.2) and *Choices of Medication* (4.4.3.3).

*4.4.3.1 Subtheme: Medications do help*

Participants reported some benefits from the medications they had been prescribed. The benefits included allowing the individual to be more active in daily life, to sleep better and to feel some sense of control over the interference caused by PDN.

*"I'd say it's probably better now since having this cocktail of drugs that I'm on" Mary, F44.*

*"I um, but the Gabapentin is always there because, sometimes I'll, I'll take a couple before I play golf." Mike, M65.*

*"I've found that the one Amitriptyline at night usually controls the worst of any pain that I do get." Barbara, F80.*

Some participants had come to arrangements with their clinicians to find a balance of medication, others had self-titrated the dose to manage any side effects. Medications had reduced but not eliminated the pain. Participants described uncertainty about their analgesic effect but were worried that stopping them may lead to the impacts of PDN becoming more intrusive.

*"… if I stop taking it [medication], it [pain] might be permanent […] because I've sort of got used to it, I kind of think 'well it must be working in some respects because I only get it, probably now I only get it about once every three weeks' or something like. So I'm of the opinion that the tablet must be doing something and I don't want to stop." Sam, M53.*

*4.4.3.2 Subtheme: Medications can fail*

Some participants had tried medications but found they were ineffective at reducing pain.

*"Just take it, you know […] three times a day, I don't think it's any good." Aaron M75.*

*"Yeah and because it wasn't doing anything to help the pain I thought, 'This is silly.'" Anne, F52.*

Some participants stated clinicians would only prescribe the cheaper drugs, and this was unfair, having paid into the system for all their working lives better medical care should be available.

*"Then she [GP] says 'right, I didn't really want to give you this one', because I think she was trying the cheaper versions first, you know, you know what doctors are like in the surgery." Mike, M65.*

*"I could go to the Doctor and say right, look, money's no object, I'll pay for these and I'm sure there'd be a Doctor out there, going yeah you can have these." Philip, M57.*

As all medications can have side effects, some participants found these were less tolerable than the PDN. Descriptions of tiredness, nausea and feeling like a zombie were common. Tension existed between symptom management and being able to live an active, engaged life.

*"…I slept all day and all night, and I felt as if I hadn't even got ... I didn't even know whether I'd got legs or feet. So, yes, they did work, but it, it just addled my brain." Heather, F57.*

*"… I was a zombie and of course when I went back to see him and told him, I said they shut everything down, I couldn't, you know they didn't do nought and he went 'well I suppose you'll have to go back on the Morphine then'." Philip, M57.*

*4.4.3.3 Subtheme: Choices of medication*

Participants had a number of points where they described making choices about medication. The options for different medications were sometimes taken in collaboration with their clinician, but some participants described medication as an imposition and presented as the only treatment on offer. Participants described situations where clinicians' choices were limited by other co-morbidities, such as nephropathy.

*"That's right I can't remember their names and I know we talked about them, but I think that was partly because of my kidney impairment, that they were felt to be inappropriate." Lisa, F69.*

Other times participants chose to refuse, reduce or stop medications that were prescribed for them.

*"If you hit the slightest nag they want to increase your medication for whatever, and um as far as I can, I steadfastly refuse to be drawn into this taking more and more tablets." Jane, F68.*

*4.5 Superordinate theme: The impact of PDN*

A schematic diagram demonstrating the diversity of impacts can be seen in Figure 12.

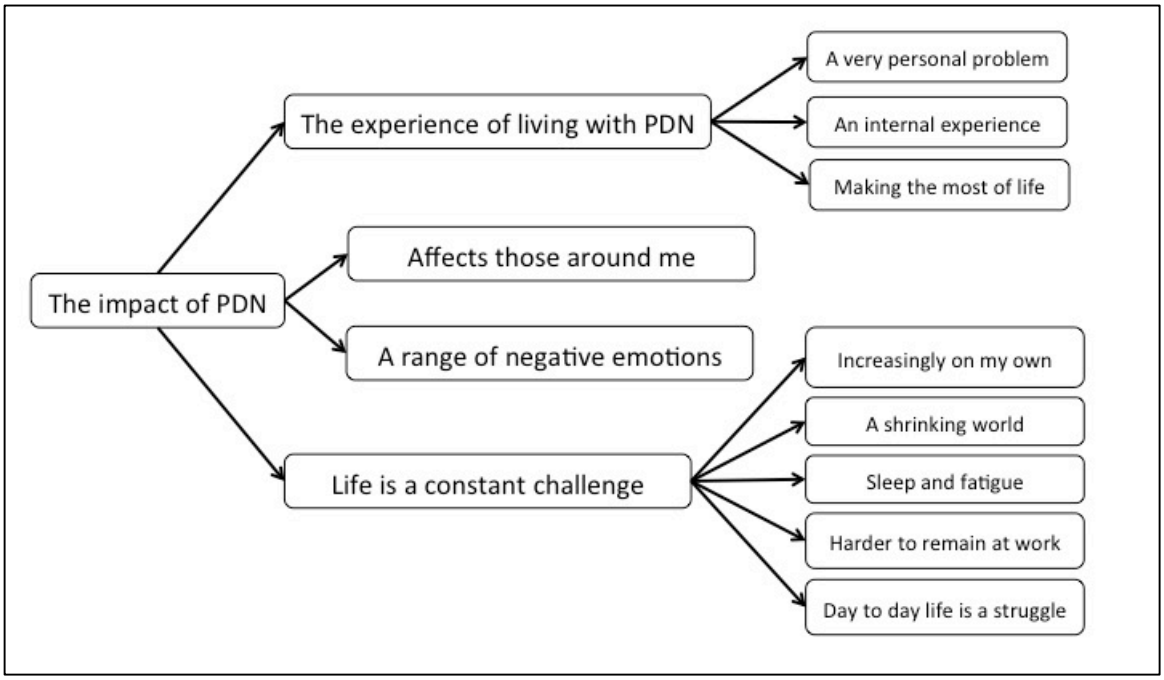
The participants described a wide variety of impacts due to PDN. For the majority of participants, most facets of everyday life were effected in some way. The quote from Joan was

indicative of the problems people faced; it is not representative of any code at this point but is used by way of introduction:

> *"As soon as it started, it made, it affected every aspect of my life, its, … you know from going shopping to going out. It has made it, … a bit, I don't know it's hard to put into words, it rules my life." Joan, F57.*

This superordinate theme contained four themes. Firstly, *The experience of living with PDN* (4.5.1) described the subjective experience of PDN. *Affects those around me* (4.5.2) described the impact PDN had on the participant's wider social network. *A range of negative emotions* (4.5.3) described the impact on mood state. Lastly, *Life is a constant challenge* (4.5.4) outlined the day-to-day impact of PDN.

Figure 12 - The impact of PDN - themes and subthemes




*4.5.1 Theme: The experience of living with PDN*

Participants spoke about the challenge of living with PDN from two perspectives. They described the personal experience of PDN. This first-person description was captured in subtheme: *An Internal experience (4.5.1.1)*. The second subtheme, *A very personal problem (4.5.1.2)*, was created to capture how participants' felt viewed by others and how their sense of self or identity may have changed due to PDN. A third subtheme *Making the most of life* (4.5.1.3) captured a counter perspective to the first two as some participants were able to carry on with daily activities despite PDN. They had a positive approach toward PDN, viewing it as a challenge to overcome.

*4.5.1.1 Subtheme: An internal experience*

There were evocative descriptions of experiencing PDN from a first-person perspective. Bob equated his experience of PDN to "Templar Torture" as there were depictions from the Middle Ages of Templar Knights having boiling oil poured over their feet in order to extract confessions.

*"…I couldn't walk at all in my job and you know it used to bring tears to your eyes believe me." Philip, M57.*

*"I went to the general GP and said look I've got these burning, burning in my feet …" Philip, M57.*

*"my husband touches my foot, and then I feel like killing him. […] I say it's like walking on hot sand." Heather, F57.*

There were some close associations with symptoms that participants described as 'restless legs'.

*"Can't keep my legs still and then they start burning, itching; oh you don't know where to put your feet." John, M69.*

One participant's pain experience affected his self-image and led him to remove all mirrors from his house.

*"I got rid of them all [mirrors], I cannot stand to look at myself." Bob, M63.*

Participants described the contradiction of having numb feet, thereby not feeling the appropriate warning pain from tissue damage, while simultaneously having an experience of burning pain that served no purpose.

*"…you get that numbness and then on the other hand the extreme pain." Bob, M63.*

There was a similar contradiction for patients, between their feet looking normal and their experience of pain perception.

*"You know what I mean, they're not gnarled and knotty, they look quite ordinary feet and yet they've got this most incredible pains." Lisa, F69.*

There were descriptions of symptoms associated with the experience of PDN such as headaches; these were more common after a stressful day due to PDN.

*"I do find I am really tired, quite stressed, always have a headache. Then I find, you know, I have problems then going to sleep." Mary, F44.*

One participant held their breath whilst trying to do a physical activity, which led to a sense of breathlessness.

> *"I find I get breathless, it's like I cannot breathe out or I'm making a cup of tea, I find I tend to speed up things. I don't know why, there's no reason to speed up." Bob, M63.*

*4.5.1.2 Subtheme: A very personal problem*

This subtheme described how participant's felt viewed by other people in society. Participants described the invisible nature of PDN, where other people could not understand what they were experiencing, or what they had to endure.

There were parallels drawn with common colds or injuries that other people had likely experienced; these shared experience allowed empathy and understanding. There were clear descriptions from participants that they kept the experience of PDN to themselves, because only someone else with PDN could understand.

> *"I'd never met anybody else with it [PDN], so ... whereas, if you've got a cold, or a shoulder pain, or something, you know, most people know what that's like. And, actually, I feel that sort of thing, people are more understanding, simply because they know what it's like, and they've got empathy." Sally, F48.*

> *"I don't think people take it seriously, they think well it's an itchy foot, get over it, it doesn't work that way." Bob, M63.*

Participants described feeling that other people had negative perceptions of them because there was nothing to 'see' that would explain the pain. If falls had been experienced, participants were concerned that people thought they were drunk or on drugs.

> *"I have fallen over a few times when I have been out on my own and people just ignored it, I think they think I'm just drunk. […] I've been laying on the floor for half an hour and things like that and people have just ignored me, I think they think I'm drunk or on drugs or something, I've never had anybody help." Kate, F58.*

From this potential lack of understanding participants had stopped talking about the problem. Instead, they chose to keep the problems they experienced to themselves.

> *"I would say "oh no it been an ok day" when actually it's been an awful day." Mary, F44.*

*"Whereas this, well, it's just, well, you know, nobody really gets it, and therefore I don't really talk about it very much, because I don't really see the point." Sally, F48.*

*4.5.1.3 Subtheme: Making the most of life*

There were participants for whom PDN did not overly affect their ability to live their lives. PDN caused minimal interruption to their lives.

*"I mean to say I do keep active, I do my own gardening all of it. I used to do all the decorating here, I don't do that nowadays I must admit now, I am nearly 80. But as I say I walk my dogs so I keep active and I think that helps because I think if you stop doing something you lose the ability to do that." Barbara, F80.*

*"I tend to ignore them [PDN symptoms], um. I just get on with life, I fish. I put my waders on. I lay floor slabs. I paint and I just get on with it and it's just part of life…well it really doesn't impact on me very much. I mean, er, I'm tending almost to ignore it." Roger, M86.*

In order to cope, and make the most of life, some participants viewed PDN as a challenge to conquer. This required being optimistic and making the most of their lives by setting and achieving a goal, or doing something nice each day.

*"Yeah, I had that sort of where I'd done something you know, I felt like I've achieved something because also the feeling of not having achieved anything, wasted a day just sat down watching TV you think what a waste of a day you know." Bob, M63.*

*"I do like a cup of coffee, and I find, sometimes, if it's getting me down a bit […] it, sort of, lifts your mood a little bit…or whatever. And I thought, that's my one pleasure, is a cup of coffee, and I'm having a decent cup of coffee." Ellen, F63.*

For Anne, this approach included not wasting emotional energy on something she had little control over.

*"What you don't do is waste it, just um feeling sorry for yourself basically, I'm in pain again, blah, blah, blah, that's no good. You've got to feed that emotion into something else." Anne, F52.*

*4.5.2 Theme: Affects those around me*

Participants described how PDN had an impact on people who were close to them. It could affect their relationships with partners and family.

*"That's all it was, and I know the type of person he [Mary's husband] is, if he feels hopeless that he can't actually physically or mentally do something he gets very worked up and so that makes the whole situation ten times worse you know" Mary, F44.*

*"I might bite Ian's head off […] and when you're a couple and somebody has got neuropathy pain, to my way of thinking there's always somebody that loses." Anne, F52.*

*"... back to, to the eighties and early nineties, it [PDN] caused a, it caused the divorce between me and my wife – she couldn't handle it anymore – and we had a divorce." Mark, M62.*

It could affect their communication and make them less tolerant to family and friends around them. Participants demonstrated this reduced tolerance by being more easily irritated in conversation or by other peoples' actions. Participants actively removed themselves from the family environment or social situations, choosing instead to be on their own.

*"It's like I said, it tends – the pain – it, sort of, takes over, um, and you might, sort of, turn around and say something, but you've said it, and you don't realise you, you've spoken sharply [...] because sometimes Keith will say afterwards, 'you don't need to say it quite like that'." Ellen, F63.*

*"I think there's just really, if my wife comes and talks to me, I say to her, 'look, I'm sorry I can't, I can't answer you, I don't want to talk to you.'" Aaron, M75.*

*4.5.3 Theme: A range of negative emotions*

Participants gave clear examples of negative emotions such as feeling angry with themselves or their feet, suicidal because of the pain, embarrassed because of social restrictions and depressed because of the on-going problems they had to cope with.

*"you know I do get bad tempered and I think why me, you know 'why bloody me?' you know. I used to like hate your feet in a way." Philip, M57.*

*"…but it must be somehow because I just get too down and I have, erm, tried to take my own life three or four times. […] Because they [medications] have to be locked away because I have taken lots of them […] Well I, I don't, I suppose by trying to take overdoses and things, I'm not coping with it." Kate, F58.*

*"I had to go out in the garden and I had to make out that I felt sick because I was too embarrassed to say about these pains in my leg because there was nothing there, there was nothing to show and our son came and picked us up and we went home." Joan, F57.*

*"Yeah, yeah, it makes me aggressive and depressed sometimes, and there are times when I go into this low mood and it takes me hours or days to come out of it." Aaron, M75.*

There were clear examples of worry about specific issues such as money and health, but often participants were generally concerned about the future, the unknown and how they may be in the months and years to come.

*"And the biggest [issue] probably, anxious problems about the future." Daniel, M67.*

Participants gave examples of frustration due to simple tasks being made more difficult or even impossible because of the symptoms they experienced.

*"I try and bite my lip and think right carry on for another half hour, and the pains that great I'm having to stop every couple of minutes, or say to them look I've got to sit down, I can't walk and I get frustrated because they're way ahead of me and then, oh, hang on, wait for our lad." Philip, M57.*

This sense of frustration linked to the next theme: *Life is a constant challenge*.

*4.5.4 Theme: Life is a constant challenge*

This was a large theme that contained five subthemes: *Increasingly on my own* (4.5.4.1), *A shrinking world* (4.5.4.2), *Sleep and fatigue* (4.5.4.3), *Harder to remain at work* (4.5.4.4), and *Day to day life is a struggle* (4.5.4.5).

*4.5.4.1 Subtheme: Increasingly on my own*

This subtheme presented the participants' reflections on their own feelings of isolation. Participants described social isolation due to cancelling arrangements or limiting their social life because PDN was too intrusive:

*"I found I was cancelling appointments, I didn't want to see people. I didn't want to speak to people, um because I thought I was going around with this tattoo on my head that I'm in this severe pain and, um, don't speak to me because I'll probably bite your head off." Anne, F52.*

*"It makes you a hermit …" Bob, M63.*

Some participants had lost confidence to go out by themselves:

*"… I just don't go out, I just don't want to go out, I can't go out. If I get out and then I can't get back because of the pain I just don't bother, whereas if he's [partner] with me he can always help me and I'm not on my own, but to be on my own outside environment just frightens me." Kate, F58.*

*"It's like I say we have got no social life whatsoever because I never know from one day to the next whether I am going to be alright to go out or not and it becomes … embarrassing and I would rather just stay in." Joan, F57.*

*4.5.4.2 Subtheme: A shrinking world*

This subtheme described the reduced scope of the participant's world. Participants disclosed that their lives had become confined by PDN, by reducing physical activity and hobbies:

*"I think I have really taken a massive step back from physical, anything physical, yeah I can't walk a long distance." Mary, F44.*

They described pain had reduced their walking capacity and tolerance:

*"… but unfortunately the pain got greater and greater to where I couldn't walk. It gave you the impression that you're walking on broken glass." Philip, M57.*

As well pain experienced when walking, participants described that reduced sensory information from their feet further impacted on their confidence to go out. Numbness due to neuropathy reduces the joint position sense required for walking and this is associated with balance issues, loss of confidence and potential falls.

*"I do fall down quite a few times, but I'm indoors or in the garden, that's not a problem, but when I go out I use my walking sticks too, for security because I don't really want to go face down in the street or anything." Kate, F57.*

As well as reduced walking, participants experienced pain and reduced confidence for using the pedals when driving.

*"It's the same with driving, sometimes when I used to drive my pick-up, if you go on a long journey you'd be in that car and some days your feet would burn that much just by keeping it on the throttle." Philip, M57.*

The combination of restrictions in both walking and driving, led people to describe losing independence, and that life had become increasingly narrow.

*"I don't know if it is because I don't drive, but in the situation I am now I do feel like my independence has kind of been, well not been taken away but I don't have as much independence as maybe I used to have because I can't walk as far." Sarah, F24.*

*"You feel to be, sort of entering this funnel where the choice is, life choices are getting smaller and smaller because of the restrictions, you know, um, you'll learn what not to do." Jane, F68.*

*4.5.4.3 Subtheme: Sleep and Fatigue*

Participants described their experiences of frequent sleep disturbance. This included difficulty getting off to sleep and, or, remaining asleep.

*"I found that I would stay up a little bit longer because the pain or the tablets hadn't kicked in or I'd get into bed, I'd go off and I'd be up at twelve and I'd be up for an hour, then it would be two hours. I don't think I've slept for more than two to two and a half hours in over two years." Anne, F52.*

*"It tends to just appear at night-time when I'm lying down, which means that it disturbs my sleep, which is the biggest impact of the lot." Sam, M53*

A common complaint was the weight of bedclothes on participants' feet. There were descriptions of how uncomfortable the lightest sheet could be.

*"Even in bed at night, the sheet is too heavy on my feet. You feel as if you'd like a cradle." Ellen, F63.*

*"I sleep in the sun lounging chair because I can't lay down because if I lay down flat it makes it even worse, I can't stand any quilts or blankets or anything on my legs" Joan, F57.*

The need to get up and walk around helped with pain for one participant, but was not conducive to achieving a restful night's sleep.

*"I can't sleep because I can't keep my legs still and the only way I can get any relief is to either stand up or walk around and even then, it doesn't relieve it, it's just not the centre of everything in your brain." Joan, F57.*

The loss of sleep quality was a key factor when describing the impact PDN had on their lives. Some participants however did not experience night pain or sleep disturbance due to PDN.

*"I have no problem with sleep, no." Mike, M65.*

Following on from sleep issues, participants talked further about the consequent tiredness they experienced during the day.

*"It's really, really bad and I'm just tired all the time, exhausted, I've totally forgotten about tiredness." Anne, F52.*

*4.5.4.4 Subtheme: Harder to remain at work*

Although most participants were retired, some were working. For those, remaining at work was a struggle due to a mixture of pain, concentration issues due to pain interference, and fatigue from frequent disturbed sleep.

*"So, sometimes I feel a bit, because I'm so conscious of my tongue feeling odd, that I do feel a little bit tongue-tied. And I, I probably don't come across that way – er, it's probably just in my head that I'm experiencing, since I'm feeling very odd – but that does worry me, you know, particularly, perhaps really for my work." Sally, F48.*

*"When it got to the stage where I couldn't walk to work and I can't go to work because I can't write, and I can't type, peeling potatoes at home has become a struggle, that's when I've realised that you know this has got to be sorted out." Sarah, F24.*

Participants described how important work was in providing and maintaining a sense of self. They described no inherent inability to do their job role, yet they had been unable to continue in work because of the impacts PDN had on their ability to cope with work demands.

*"I think it was also thinking work are sort of seeing it like 'oh you're not coping you're not managing' and when you're so used to being in control of things it's very hard to then have people saying '[name] we think you should cut your hours in half' or 'we think dropping down a band so you haven't got that responsibility'." Mary, F44.*

*"I haven't got to get up and get down for work for seven o'clock in the morning, no, so it's you know, you can sort of cope across with that." Lisa, F69.*

As a counter point, there were participants who were employed, and did not find PDN affected their ability to perform their role.

*"I've never, pretty much ninety-nine per cent of the time, never suffered with it when I've been at work or volunteering…" Sam, M53.*

*4.5.4.5 Subtheme: Day to day life is a struggle*

This subtheme was constructed from participants' descriptions about unique impacts of PDN. These were separate and distinct from impacts outlined in subthemes so far. This subtheme demonstrates the breadth of impact PDN had on everyday activity.

The impacts include the physical difficulty of getting up in the morning after a night in bed:

*"Then as soon as you get up in the morning, as soon as you put your feet down on that ground it kicks off." Philip, M57.*

The affect PDN had on memory and concentration:

*"Well I'd say my memory is awful. I can remember things quite away back, but things I've done a couple of days ago just go, they just don't stay in my head." Kate, F57.*

The difficulty participants experienced simply sitting still - they were unable to sit through a film or dinner with friends, without needing to get up and move.

*"I am sat down now in a chair and that is my worst part is sitting down …" Clive, M86.*

They described how the experience of PDN could make them feel nausea so affecting their appetite for food. This had a subsequent impact on diabetes dietary management.

*"… I'd feel physically sick with the pain, I wouldn't be able to eat which obviously then in turn affected my blood sugars, it wasn't very productive for my diabetes to be feeling that way." Sarah, F24.*

Participants disclosed their intimate relationships with partners had diminished or ceased because of PDN.

*"Definitely because I get it up in the groin and when it's in the groin it's like having a gnawing toothache, so I think there's probably a lot of people that wouldn't want to say, "I don't have a sex drive, I don't feel sexy anymore. The desire's just …" I mean I*

*love my husband desperately and we've got a great relationship, um, but I miss the closeness because there's something about that final closeness that you share that is just between you two that you don't get anywhere else." Anne, F52.*

Because of sensory loss, participants were aware of the need for foot care and surveillance. Closely allied to this, some had problems buying appropriate fitting footwear.

*"Not really, I mean I, I am very aware of my feet as a diabetic anyway, so I do wash them daily and check them regularly and I do get my husband to look at them underneath, the bits that I can't see to make sure they're alright and I do wear sort of clean socks or tights every day." Lisa, F69.*

*"Um that you can send off for it [shoe insoles], it saves you going looking round shops and they make these shoes, you know like the idea of a mattress, that moulds to your body." Jane, F68.*

Participants reflected how life had altered since they developed symptoms of PDN; they particularly focused on lost independence and how their personality may have changed.

*"I used to be the life and soul of the party, feisty, bolshie, er, confident but now I'm just you know basically a shadow of what I was before." Bob, M63.*

*"I used to love walking, um, and standing because I've always done baking and I've always been an active person in respect I'm always on my feet." Anne, F52.*

Participants spoke generally about the restrictions to daily activity they faced without being specific; the implication being that all aspects of life were affected by PDN.

*"Well, it stops us just doing day-to-day things […] So I, basically all the things I used to do, I don't do." Neil, M66.*

*"You try and get across what this pain does to you, it's a depravity, is that the word?" Anne, F52.*

*"I've had to have treatment for my eyes, for retinopathy and things like that, kidneys are okay, but it's, I guess it's the neuropathy that is so intrusive and painful at times." Dawn, F68.*

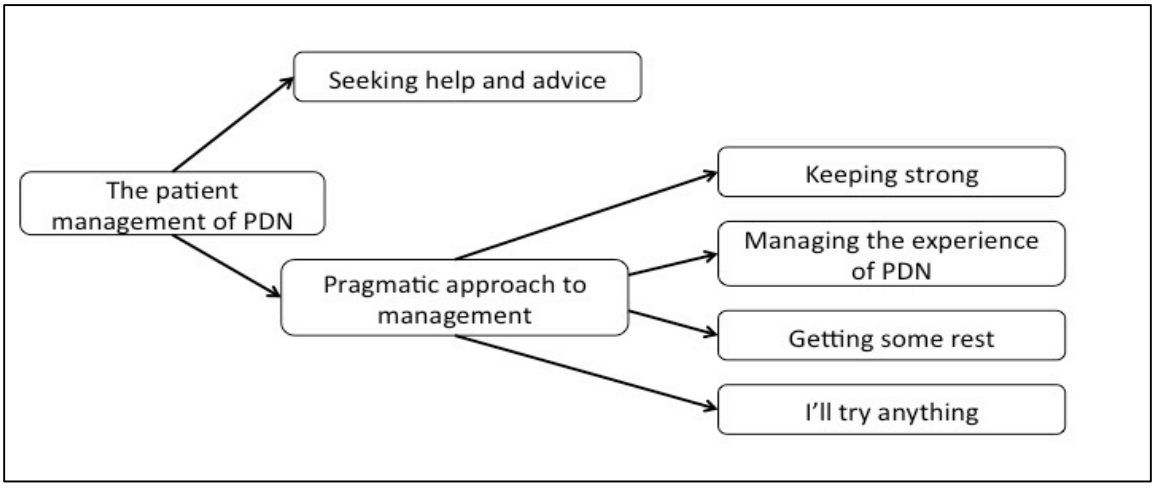
As Dawn suggested in the last quote, although she experienced other complications due to her diabetes, it was the PDN that had the greatest impact on her life.

*4.6 Superordinate theme: The patient management of PDN*

The participants in this study described a wide variety of management strategies they had tried. Any strategy, whether successful or not, was grouped into the following themes (Figure 13). These strategies were in addition to the advice for PDN management that they had received through the NHS services that were described in section 4.4.

This superordinate theme contained two themes: *Seeking Help and Advice* (4.6.1), this described the sources of information that PDN participants had accessed. The theme *Pragmatic approach to management* (4.6.2) described the variety of strategies participants had experimented with to manage the impacts they experienced.

Figure 13 - Patient management of PDN - themes and subthemes




*4.6.1 Theme: Seeking help and advice*

There were very few instances when participants described specific points of information and help they sought regarding PDN. No participant was explicit about an issue or topic they had researched rather, when this issue was raised, participants wanted general information.

*"As much, as much information as possible." Ellen, F63.*

Participants had often used the Internet to seek information. There was scepticism about the accuracy and veracity of Internet pages. Participants were cautious about any site that claimed 'miracle' benefits or charged for supplements.

*"I Googled it, there was a company in North America that was selling these vitamin B, extra strength vitamin B, and I took that for a while, which I suppose did help, I don't know if it really helped that much or not." Dawn, F68.*

*"you can never be sure that you are getting what you are paying for and you don't know what is in it, and you know they always say you know the best person to prescribe your medicines is your GP." Joan, F57.*

The Internet had led some participants to peer-support forums. There were both positive and negative experiences of accessing these forums. Participants found reading the experiences of others with PDN created some validation of their own experiences. They described feeling less alone and isolated and benefited by hearing how other people were coping.

*"I think I was looking for somebody else with the same sort of problems I was having, it just felt good to know that actually even though you're here, and there isn't anybody else I know close to me with diabetes, with the same problems […] they're all around the country and they're all experiencing really a mirrored image of what I'm going through." Mary, F44.*

Some forum users were less helpful though, posting replies that implied development of PDN was due to poor diabetes management and suggesting that it was the individual's fault.

*"…you'd only get the odd few who that would say 'well actually I don't know, you've done something wrong' and you think 'well why post that on there?'". Mary, F44.*

There were two characteristics for the sources of information that participants trusted; firstly, they wanted clinicians to provide accurate information and treatment. Some participants posed questions during the interview relating to adjunctive treatment such as magnetic socks or herbal remedies, they had seen advertised. Secondly, they prioritised information that came from significant others, this was both from important people in their lives such as partners and close friends, and from other people who experienced PDN first-hand. The role of others and the support they gave has been included in the superordinate theme: *Perspectives on talking therapy*.

### *4.6.2 Theme: Pragmatic approach to management*

This theme contained four subthemes: *Keeping strong* (4.6.2.1) described how the participants mustered internal strength to 'keep themselves going' with PDN. *Managing the experience of PDN* (4.6.2.2) collected all strategies participants explored to reduce the experience and mental burden of PDN. The subtheme *Getting some rest* (4.6.2.3) collected all strategies employed to minimise fatigue and maximise sleep quality. Finally, *I'll try anything* (4.6.2.4) captured all other strategies employed.

*4.6.2.1 Subtheme: Keeping strong*

A common account from participants was that it was difficult to cope with PDN. The impacts on many aspects of life were pervasive and draining.

*"I don't know how I cope really, I just, you just have to get on with it." Kate, F58.*

There were a number of ways by which participants resisted the imposition of PDN. Mark described building a wall around his pain, trying to blot it from his perception.

*"I try sort of, say, 'no, I'm not suffering pain', blot it out, build a wall around it, block it away." Mark, M62.*

Participants used strategies to remain in control; these strategies could be passive:

*"I hate going out, and it's all to do with building up a castle around you where you've got some measure of control is the word." Bob, M63.*

The strategies could be more active, maintaining a sense of self by putting on make-up and looking your best, despite PDN.

*"I just felt that was a part of me I could control I could get up, will brush my [hair]… you know I will dress nicely when you don't feel like doing it but that was me something I could do." Mary, F44.*

Maintaining this strength did not come easily. Participants described ways of seeking motivation to continue with the effort.

*"I try and motivate myself. I'm always continually looking at power of motivation. I continually look up motivational quotes wherever I can find them, use them examples." Daniel, M67.*

Participants described reappraising and revising their expectations of themselves and their capacity for work, to maintain a positive outlook and avoid a sense of failure. There was language of accepting they had this problem, and achievements of any size should be looked at positively for the accomplishment, rather than compared to how they might have been without PDN.

*"You know the things and the places will always be there, they will be there the next day so if you don't achieve something today there is always tomorrow." Joan, F57.*

*4.6.2.2 Subtheme: Managing the experience of PDN*

All participants had experience of drug treatment aimed at reducing the experience of PDN. This approach had been beneficial for some (Section 4.4.3). Participants had explored a variety of alternative ways to reduce the pain they experienced. Because PDN was often described as a 'burning' sensation, the use of cold was a common approach. Participants had used topical menthol gels that gave a cold sensation, cold water baths to soak their feet, and a draft to blow across their feet. One participant, when living in Canada, walked out into the snow at night to try and get some relief from the pain.

*"I had to have the fan on all night on the feet just blowing cold, cool air on my feet and sometimes getting a frozen pack of peas or something like that" Aaron, M75.*

*"And it's cold water straight out the tap, and I stick my feet in it until the water goes warm." Heather, F57.*

*"In Canada, I was out in the middle of winter in, in just my slippers and pyjamas, trying to focus, so that I could get to sleep". Mark, M62.*

Most participants found the beneficial effects were short lived, only while the cold sensation lasted. Participants had also tried warmth, using warm water baths or hot water bottles. Again, they found the benefits were temporary.

*"Well I have done that, but you can't put your feet in warm water for eight hours a day. I've done it when it's that severe, I've tried it." Philip, M57.*

Although participants had described the painful sensitivity to light touch they experienced, some found massage to their feet, either by themselves or their partner, could be beneficial.

*"It's probably going to sound really stupid but I do find that rocking or brushing my feet on the bed linen, I find that comforting. I don't know if it stops the pain but I think it's comforting" Sarah, F24.*

*"Basically um, massage the area with really firm, not just stroking the foot, but really, almost with my fist." Dawn, F68.*

*"My wife massages with some oil and my feet feel a lot better and I can walk a bit better." Clive, M86.*

As well as physical techniques to their feet, some participants had made adaptations to their home environment to aid with day-to-day tasks. Acquisition of equipment allowed

maintaining a level of function and independence. Maintaining a level of function in the home was integral to another common strategy - keeping physically occupied with day-to-day tasks and so distracted from the pain they experienced.

> *"I find if I sit down or a lie down to ease the pain with, that I can do with the chronic pain, that doesn't work with the diabetic neuropathy. And I've found that the best form of, of controlling it is, is keep myself busy." Mark, M62.*

> *"I feel that in the day my brains got plenty to think about and do and I'm looking at things and doing things and um involved in things of all sorts of different, different things in life and it's fine." Lisa, F69.*

Similarly, participants found mental distraction techniques useful in focussing their attention away from the experience of symptoms.

> *"I use a distraction technique of various methods. One, one I use often, is I imagine I am winning sums of like one hundred and eight million pounds on a lottery and how can I make peoples' lives better out of that money? And then another day I might think I'd just won twenty thousand, other days it might be sixty thousand and that will actually take me about an hour after my walking." Daniel, M67.*

> *"Then I'm thinking, remember the ocean and blue sky and how it really, really rained. Immediately when this [pain] is going 'bang, bang, bang' like this, I'm over here thinking the very first time I took the children to Stonehenge when they were small, the very first time I drove to Cornwall on my own with them in the car. I think of all the little things that are trapped somewhere in my memory and they bring them out." Anne, F52.*

#### *4.6.2.3 Subtheme: Getting some rest*

Fatigue and sleep disturbance did not affect all participants; there were some whose sleep was unaffected (Section 4.5.4.3). However, when present, the impact on sleep and rest and the consequent difficulty with tiredness and concentration were significant, but participants had received no advice for sleep or rest strategies.

There were various strategies explored by participants to manage their downtime and sleep quality. They used rest from physical activity to manage the pain that the physical activity may have aggravated.

*"I sometimes can go and make a cup of tea and sit down for ten minutes, because you know, you've got to take, just, just rest yourself." Mike, M65.*

*"I have to sit down and rest because they [feet] really, really hurt […] he's always there to sort of hold me up and say, 'oh, we'll sit down for a little while and that.'" Kate, F58.*

There were specific references that going back to bed or staying in bed was the least-worst option, but these approaches did not remove the neuropathy pain completely.

*"Ian will tell you when I say to him 'I'm at collapsing point', I just have to collapse on the bed and I have to let the tiredness take over." Anne, F52.*

*"I think, oh, well I'll go to bed, you know just lay in bed, read a book or listen to some music, but you see you're not free from the neuropathy." Philip, M57.*

Participants described experimenting with a range of relaxation strategies to manage pain, and then continuing with these regularly because they were useful. These strategies included listening to music, visualization techniques and body scan techniques.

*"I'll put the music on and the headphones on. Then, before I get to that stage, I'll put the music on and I will really try to calm down, it doesn't always work." Anne, F52.*

*"It's almost like I'm visualising a big block of, like a block of ice or a block of stone, which is the pain and visualising that and just chipping away at it and it does start to you know, if I've got myself in a kind of nice state of thought and concentration it sometimes works so I would say that is definitely a method that I use well." Sam, M53.*

Participants described using breathing exercises as an active relaxation strategy to help them manage the pain they experienced. All these participants had experienced contact with psychological services, either specifically for the PDN they experienced, or as part of a PMP for persistent LBP.

*"I get the shakes when I can't … it gets like this and my body will tense and I have to do my breathing exercises […] I would relax back on the pillows, I would take a deep breath in, I would slowly let it out and then I would breathe just like that. I would try and let the neck go and shoulders go and take it right down the arms till, um, I start*

*feeling like okay, I'm feeling a bit more gelled [chilled] now, I'm not feeling so tense." Anne, F52.*

*"You concentrate on your breathing for a little while very deeply, err and it takes your mind off other things that are happening in your body." Barbara, F80.*

Other participants were aware of relaxation but had never applied it consistently with the aim of managing their pain. Others had difficulty implementing the advice they had received, usually due to family or work pressures precluding protected time to experiment.

*"Um, the ones where you, you know, you need at least ten minutes, and to be in a quiet place, and to be very focused. She provided me with the tapes, different sorts of, um ... You know, somebody talking about, you know, visualise a red spot, kind of thing [...] No, not really. I mean, I will occasionally do it, and sometimes, at night, I do force myself to [relax]." Sally, F48.*

There were frequent references to sleep strategies. Some participants had been prescribed specific sleeping tablets, but often did not tolerate the side effects the next morning. Participants described a routine for bedtime that included avoiding caffeine, some form of relaxation and time to wind down from the day.

*"I'll just try and unwind and I might read for like five ten minutes because usually find I can relax quite a bit if I read so most nights I do tend to read once I'm in bed." Mary, F44.*

*"I always try and work the same routine. I've usually sat down for an hour or so, maybe a bit longer of an evening, watching television. I always have a milky drink last thing at night. I always take my dog out for about 10 minutes last thing at night, then she gets put to bed with a biscuit and I take myself upstairs. I do the same thing every night." Barbara, F80.*

Because of the sensitivity from the sheets, participants questioned why no one had designed some kind of cradle to lift the sheets from their feet. Some participants had to get up and walk, they would rather experience the pain from walking, but this choice had clear impacts on being able to achieve a restful night's sleep.

*"…the only way I can get any relief is to either stand up or walk around and even then it doesn't relieve it, it's just not the centre of everything in your brain." Joan, F57.*

*4.6.2.4 Subtheme: I'll try anything*

This theme captured the diverse range of techniques participants had experimented with to manage their PDN. They had tried electro-acupuncture pens, chiropractic treatment and machines to stimulate circulation.

> *"What it is actually is acu-stimulation and it's sort of electric pulses given to certain parts of the ear. In the same sort of principal as acupuncture." Sam, M53.*

> *"And we went there and we laid on this thing and he pummelled your back and whatever and they did it say for £37.00 at first and then of course it went up to about £300 and odd and I said no I am not paying £300 and odd. […] No I don't think it did make a difference." Clive, M86.*

Bob was a particularly experimental, trying cling film wrap, fish pedicures and walking on stinging nettles:

> *"I tried strapping them in cling film. […] I tried the little fishes in the water." Bob, M63.*

> *"The most potent thing I've tried to work was stingy nettle funnily enough. Yeah, I'd take my shoes and socks off and I'd walk in stingy nettles tended to take away the other pain temporarily. It didn't work long-term but that's how far I was prepared to go to try anything." Bob, M63.*

Participants described experimenting with legal drugs such as alcohol. There were some benefits, particularly as an aid to sleep, but they were conscious of the difficulty in balancing the benefits with potential negatives of over-reliance and addiction.

> *"It would be so easy just to get a bottle of Scotch and drink it." Mark, M62.*

One participant had experimented with cannabis but found it no use.

Perhaps because people had experienced less than optimal success with medication, and there were few other strategies being recommended by HCPs, participants explained they had no option but to experiment with anything that may be of benefit. Despite wide ranging attempts, the participants had found little benefit from any of these diverse approaches.

> *"You get sometimes to the point where you think, I'd try anything...?" Ellen, F63.*

They generally took a pragmatic approach to these strategies, that was best summarized by this quote from the code *Doing what works*:

*"Well, that's it - what works for one doesn't always work for somebody else." Ellen, F63.*

*4.7 Superordinate theme: Perspectives on physical activity*

There is a distinction between *physical activity* required for day-to-day life, and *exercise*, which is structured physical activity undertaken with the aim of improving health. The interview participants did not necessarily make this distinction and so this theme considered their perspectives on physical activity and exercise as synonymous.

Due to pain and loss of sensory awareness, participants frequently described uncertainty with walking and fear of falling (Section 4.5.4). To mitigate these fears and maintain a tolerance for walking, participants had adopted walking aids for balance and a sense of safety.

*"I walk with walking sticks when I'm out because I'm always falling and I suppose it's because of the pain and I don't always recognise where my foot is" Kate, F58.*

*"I always take my stick with me now, always and I just feel a lot safer with that so if I do have that wobbly minute, I've got my stick if I'm not holding on to anything else." Mary, F44.*

Some participants had purchased or been provided with mobility scooters or wheelchairs. There was some reluctance to use these as they were viewed as a further sign of disability.

*"I miss steps and things like that. Sometimes I have to use a wheelchair, but I try not to, but I sometimes have to resort to that" Kate, F58.*

But there was an understanding that these aids allowed potential walking distance to be extended, facilitating opportunities for time away from the house.

*"If it's wheelchair, it's wheelchair, you know?" Ellen, F63.*

*"I'm using a wheelchair now to get from A to B, to go that distance." Mary, F44.*

Some participants described specific exercises done to maintain their physical health. The aims of the exercise were variably to maintain strength, fitness, standing balance or body flexibility.

Some participants had been advised to use resistance bands or go to a gym to maintain strength.

*"I sometimes do a bit of exercising with elastic, you know those long elastic straps. I try to do that. And again that's done in a routine, I do so many above my head, so many across my chest and then that's packed up and put away." Barbara, F80.*

*"I'm even in discussion with the doctors, they have said that you know going to the gym and being, staying active, and doing what I can when I'm there may help with obviously kind of, well not muscle wastage but losing the strength." Sarah, F24.*

Sarah was the youngest participant and at the time of interview was off work due to her PDN symptoms. She described her reluctance to go to a gym and potentially be seen out in public whilst deemed not fit for work.

*"I'm starting to get a little bit better about going out during the day when I would normally be at work" Sarah, F24.*

One participant had taken up cycling because this allowed her to maintain cardiovascular fitness in a manner that did not aggravate the pain as much as walking and it provided some focussed distraction.

*"Cycling up hills, or dealing with traffic is a distraction from maybe thinking about my feet, whereas walking around ... I used to do a lot of walking – less so since I've moved to [city] – but, when I was younger, I did loads of fell walking." Sally, F48.*

Primary care exercise-on-referral schemes were not felt to be targeted towards, or inclusive for PDN.

*"You get GP referral [exercise schemes] but obviously that's when you've had broken limbs or, or strokes or things like that, they all do that, but nothing else. I would be the first on the queue if there was some sort of programme like that." Lisa, F69.*

Mary had been advised some exercises using a physioball to maintain balance.

*"Sitting on the ball was from sort of the physio that I had quite a few years ago to try and help my balance." Mary, F44.*

The most usual exercises described were ankle rolls, to maintain some flexibility and movement in the lower legs. Participants had not been advised to do these movements by clinicians, but had initiated them independently feeling they were potentially helpful and unlikely to cause damage.

*"I do sit and do some exercising of my feet when I'm sitting down at times […] Yes, and try to keep the muscles going there, but I'm sure that I'm not doing all I should do or couldn't do, but I don't know what else to do?" Lisa, F69.*

*"I am just moving my legs now, you can't see them, but I am moving them just to get them going, but the pain is there." Clive, M86.*

Participants described feeling better for having completed some exercise and achieved positive health benefits.

*"Actually you get this sense of achievement don't you, you know, if you've done sort of three quarters of an hour, um physical exercise, where you'd be just sat at home maybe doing nothing. […] It's as if exercise actually overrides everything that you feel, I'm conscious of this pain nearly all the time, but I'm distracted, if I'm doing something." Jane, F68.*

Participants expressed concern about losing their physical fitness and function over the years and some did engage in general exercises, within the limits of their pain, to maintain their health as best as possible. However, no participant had been given specific advice for exercise that may have beneficial effects for their PDN, nor had they been advised of exercises that were to be avoided. This led to uncertainty about how best to approach exercise, with PDN.

*"Um nobody's ever said yes, you know, you could do things like exercises that would help or anything like that, so I, I've never, never really um looked at it". Lisa, F69.*

*"It [exercise] is a big thing and I think a lot of people most probably would want to do it in an almost in a controlled [manner], so there would be no way I would next week go off to my local gym and start [exercising]." Mary, F44.*

From this uncertainty, the participants who did want to be more active wanted specific guidance from HCPs about appropriate and safe exercises for PDN.

*"Then if that's a sort of an achievable thing to do, then okay you start off with just one minute, but you can work up to five minutes, but you know you're doing the right thing, I think guidance like that would be useful." Lisa, F69.*

*"I'd say it's sort of up there as being very important I'd be more than happy if somebody came along and said 'Right, we're doing this.'" Mary, F44.*

One participant had specifically researched the role of exercise for the PDN, and was pessimistic about the likely benefit.

> *"Well, I've read up on this thing quite wildly, I've read up on the type of exercises you can do, some of the foot exercises you can do, some of the strategies you can use and I've tried many of them, I need to you know, the way I look at it, this pain originates from the damaged nerve and there is nothing you can do about nerve pain". Aaron, M75.*

In summary, some participants were frustrated they were unable to be more physically active. Pain was the common limiting factor. Although some participants had made adaptations to their expectations of exercise type and intensity, they were able to achieve or manage less activity than they wanted.

There was uncertainty about how best to approach exercise, particularly anything that maybe specifically aimed at reducing or managing PDN. Participants had not received clear guidance, other than standard foot protection advice given to all people with diabetes. The desire to be more active was not universal amongst participants but those who did want to be more active wanted clear advice from clinicians. A competing view existed that pain was due to nerve damage, and there was no mechanism by which exercise could improve this situation.

### *4.8 Superordinate theme: Perspectives on talking therapy*

Of the twenty-three participants, two had received psychological therapy input specifically for PDN and one had attended two PMPs (UK and Canada) for persistent LBP. The majority of participants had not discussed psychological support with their HCPs.

This superordinate theme contained two themes: *Open to talking therapy options* and *How can talking help?*

#### *4.8.1 Theme: Open to talking therapy options*

There were a number of key areas participants discussed positively in relation to talking therapy. For some participants, there was openness to the idea that psychology and mood state were directly relevant to the issues of PDN. Participants described help to manage mood and help to manage stress as the areas where talking therapy maybe most useful. They described partners and other people who experienced PDN as most valued for discussing and sharing these issues. Lastly, professional psychological help had been found useful but the difficulty in accessing psychological services through the NHS was raised.

Some participants came to a realisation that the problems they experienced due to PDN, were more than pain and physical impediment. Their experience of particularly unhelpful moods and their reactions to stressful events, made them approach medical services to access psychological therapy.

> *"I would say that I probably took the first step into asking for some help and guidance, it wasn't offered to me, and then it was 'oh yeah, actually I think I might need to speak to someone because I'm feeling a bit low about how I was feeling'". Sarah, F24.*

> *"Um, I think, I think the psychological impact is probably the next thing, really." Sally, F48.*

There was awareness that moods were difficult to manage and had a negative effect on overall quality of life.

> *"I think the management of mood would be quite useful and how to cope with that because um, it's just incredibly wearing at times." Dawn, F68.*

Similar to other persistent pain conditions, some participants had identified life stress as an aggravating factor: stress from living with PDN, from relationships and work were identified as issues.

> *"I think if you can understand what the stress is about or what has caused that stress in the first place, you can manage it better; therefore, you can understand it better." Anne, F52.*

> *"And plus the fact, I find stress aggravates it [PDN]." Heather, F57.*

> *"I also enrolled myself on a six-week group course that was about stress and mood management, which has been quite helpful." Sarah, F24*

Participants viewed being able to talk about the issues experienced or the causes of stress positively. Some found close family members, especially partners, to be best at listening and understanding. Other participants did not want to burden their partner further and preferred being able to talk to a friend who might be more objective.

> *"… he has seen it since it started [PDN] and he is my husband, he is my best friend, so him being there reassures me, there is nothing that I could tell him that he wouldn't judge me for." Joan, F57.*

Some participants had accessed psychological support specifically for PDN. They viewed this opportunity positively for the affordance it provided to discuss the impact of PDN with a neutral professional; they felt professional detachment was beneficial and more appropriate than discussing the issues with either family or friends.

> *"That feels quite good, being able to just be somewhere else, talking to somebody else. I think that's quite good for some of my stress, but it doesn't help with the pain of course, but just being able to talk to somebody different because I've no idea of anybody who lives in this area, I've got no relatives or friends here". Kate, F58.*

> *"I could really have done with talking to somebody [psychology] who is totally distant, they're not family members, they're not my GP who hasn't got the time for you to sit there and like off load to him so it is quite nice sometimes." Mary, F44.*

The professional perspective of a psychologist had helped Sally to reappraise the implications (amputation) she feared about the symptoms she experienced (pain).

> *"I think the single most useful thing that she pointed out to me was that for me, the problem was not the pain, it was what it symbolized [potential future amputation]." Sally, F48.*

Psychologists often use CBT models for their consultations with patients and this holistic approach had been useful to make links between the psychological and the physical process:

> *"we did a little bit about [CBT] and we spoke about behaviour patterns and the unhelpful thinking that people have in general and obviously how I can change the way that I think. I mean it has been really helpful to hear from someone else's perspective." Sarah, F24.*

As well as family and friends, participants described there were, or could be, particular benefits in talking with others who experienced and so understood the impact of PDN.

> *"Yeah, knowing what other people are going through the same thing." Bob, M63.*

> *"…maybe through talking to other people who do experience it, [is] something I could benefit from." Sally, F48.*

> *"…nobody understands what I'm going through unless it's another diabetic or it's somebody else suffering neuropathy because they're going through the same thing." Philip, M57.*

One participant had attended PMPs both in Canada and the UK for management of persistent LBP. Although not specific to neuropathic pain, he had applied the strategies from these PMPs to the impacts of PDN he experienced.

> *"I would advise if anybody that suffers with this diabetic neuropathy, if they can get down to a pain management course, take it. […] Okay, relaxation, exercise, all the things that I do with the chronic pain, applies to the neuropathy." Mark, M62.*

There were issues with accessing talking therapy, whether family or peer support. Dawn lived alone in a small isolated village and noted the absence of someone to talk things through with. The demand for psychology services within NHS Trusts meant there were waiting lists so access was not as timely as might be hoped for.

> *"I have to say I live alone so you know, talking it through with anyone, well I suppose that might help actually, but I live right out in the sticks so there's not actually anyone here." Dawn, F68.*

> *"Bearing in mind even though we have two [psychologists] that we use for the diabetes clinics, they are also used for the whole of the hospital so there's quite a long [wait list]." Mary, F44.*

*4.8.2 Theme: How can talking help?*

In a counter view to the previous theme, not all participants were open to the idea of psychology. They were very clear that PDN was due to nerve damage and not effected by mood state. They did not want advice from other people, particularly those who did not have PDN and were not keen on any form of talking therapy.

There was a strong view from some that talking about PDN and its impacts were not appropriate - how could mood state affect the pain experienced from nerve damage in the feet?

> *"But I don't know, my pain is my pain, I don't see how anyone else can help with it, I've had it now for four or five years and I'm coping with it the way I can". Aaron, M75.*

> *"I've been offered them [counselling] by the doctor, you know, if you want to see someone, you can talk it through, or what-have-you. I don't know if I believe in that sort of stuff. […] I can imagine me hearing something that sounds absolutely crazy to me, and, you know, I would, I'd be the sort of bloke that would say, 'oh, pull the other one'." Neil, M66.*

Neil went on to say his perspective of talking therapy was changing. He was now severely disabled by the pain he experienced and that he may be willing to try different approaches.

*"When you get more desperate (laughs), you begin to think, well, it wouldn't hurt, but would it help?" Neil, M66.*

Participants wondered how counsellors or psychologists without PDN could understand the health problems that they had to cope with.

*"Just because she has been through university and think that she knows everything, I just said you know, she won't know how to cope with my problem. You see these young people around, social workers and so on, they have no practical experience." Aaron, M75.*

The contribution of peer-support groups had both positive (in the previous theme) and negative opinions. Lisa felt that peer-support groups would not provide the support she was interested in and, if she were to talk to someone they needed to be a medical psychiatrist, otherwise it would not be 'proper'.

*"I don't want to go to, self-help groups I think [they] are a load of old biddies sitting round going 'oh well, I take these tablets, well I take those, oh these are better' and I think 'no, not interested'. But if it was something that was, professionally led, that's a whole different ball game and I can, I can accept that." Lisa, F69.*

*"I'm afraid I'm traditional medicine, I'm afraid, I don't, um, you know to me it, [sigh] I don't like the thought of any sort of quackery medicine coming in if you […] if I spoke to a psychiatrist I'd want to know he was a properly qualified, not one of these pseudo-psychiatrist [laughing]." Lisa, F69.*

One participant simply found talking to people who were not her immediate family difficult, and could not conceive of attending any kind of group programme.

*4.9 Results summary*

This study used qualitative interview methods to investigate the impacts people experience due to PDN. It found substantial impact on many aspects of day-to-day function and quality of life. The strategies people used to cope with PDN were also explored. Participants reported variable benefit from medication which led them to explore a wide range of strategies aiming to minimise the experience and impact of PDN. The degree of success of these strategies was individual. Lastly, this study explored whether people with PDN felt PMP strategies might be

appropriate to help them cope with their experience. There was uncertainty about physical activity parameters, and some people wanted specific guidance of what exercise to do and what to avoid. There was ambivalence toward psychological therapy with some positive perspectives based on previous experiences but also strong views that PDN had nothing to do with mood state, and hence targeted psychological approaches were inappropriate.

## *4.9 Discussion*

### *4.9.1 The issue of PDN impact*

What was previously known about the impact of PDN has been outlined in Chapter 1. This introduction highlighted that PDN is painful, makes walking, standing and general activity more difficult. Sleep quality and mood states are generally worse in people with PDN compared to people with diabetes alone (Collins, Corcoran and Perry, 2009; Reddy *et al.*, 2010). These previous studies used questionnaires to gather data, most commonly the BPI, NeuroQOL, MOS, HADS, SF36 and EQ5D (Alleman *et al.*, 2015). The construction these questionnaires have a restricted range of questions and responses.

This interview study has demonstrated that PDN has a more wide-ranging impact on many aspects of physical, cognitive and social function than previous literature suggests.

To look at one outcome measure in greater detail, the BPI asks respondents to consider seven domains: general activity, walking ability, sleep, life enjoyment, mood, normal work and relationships with other people. The diverse range of impacts found in the current study makes simple categorisation into one of the above difficult. The theme *A range of negative emotions* included participants' accounts related to the experiences of worry, frustration, anger, depression, embarrassment and thoughts towards suicide. The BPI requires the respondent, who may well have a range of these emotions outlined above, to condense this emotional range to be reflected in a single answer.

The BPI contains one scale for Interference of pain. The subtheme *A shrinking world* contained codes including *losing mobility*, *stepping back from physical activity*, *losing independence* and *had to stop driving*. It was appropriate to bring these descriptions together in the study analysis and to reflect them as a higher-level theme, but again, it would seem challenging to capture these diverse impacts accurately on one BPI interference scale.

This is not to suggest that existing quantitative research studies are of no benefit, rather this study adds the personal insight to the experience of living with PDN. Questionnaire outcome measures delineate the questions asked and the potential responses. This allows analysis at the

population level, but maybe less than ideal at the individual level (Kerry *et al.*, 2013; Anjum, Kerry and Mumford, 2015).

Participants described impacts that are not captured by existing questionnaires including a sense of isolation from their close family and local community. This impact is present within the theme *Affects those around me*, where participants described withdrawing from their family when pain flared up. Also subthemes: *A shrinking world* where people had less independence and self-determination than they wished, and *Increasingly on my own* where people described struggling to maintain a social life and being socially isolated.

It has been suggested that the unpredictable pattern of neuropathic pain can be a factor leading to social isolation (Closs *et al.*, 2009). This pattern is in contrast to other pain mechanisms, for instance osteoarthritis inflammatory pain often has a diurnal pattern which allows people to schedule social and physical activity (Smart *et al.*, 2012a). This predictability can allow some control over the impact of pain. In contrast, the lack of predictability that characterizes neuropathic pain does not allow control by activity scheduling (Daniel *et al.*, 2007).

In a study with older adults with neuropathic pain (60yrs+), the main causes for social isolation were perception of physical limitations and uncertainty about how pain symptoms would react (Sofaer-Bennett *et al.*, 2007). The limitations included being unable to participate in physical activity such as days out and feelings of reduced self-esteem. Uncertainty included the potential to have disturbed sleep the night before, and to be feeling more anxious and less confident. Although this sample (n=16) had diagnoses of neuropathic spinal pain and PHN, there were clear similarities with the current study population.

Participants in the current study were very clear about the hidden nature of PDN (themes: *A very personal problem* and *An internal perception*) and this added to their sense of isolation. The participants often did not know anyone else with PDN. While they may be aware of friends and family who were diabetic, they did not have peer-validation for their experiences of PDN. This hidden nature, where they had significant levels of pain but their feet looked normal, was a conundrum or paradox to them. The apparent inconsistency between subjective experience and objective 'reality' led some people to keep the problem to themselves. They expressed concern about what wider society thought of them. If they were unable to explain to themselves how their feet looked normal but hurt, how could they explain this to others?

These themes of isolation and concern with societal opinions have been mirrored in other qualitative studies with people who experience persistent pain. Closs *et al.* (2009) found many relationships had been negatively affected by lack of understanding from others, particularly

around pain severity and associated disability. Non-specific LBP is often associated with a lack of clear causative structural factors and this diagnostic ambiguity has led people to feel stigmatized by others (Smith and Osborn, 2007; Slade, Molloy and Keating, 2009). People with LBP perceived others in their work and personal lives to imply they maybe malingering and seeking financial gain from their pain. In order to avoid these situations the person would stay home and reduce their engagement with society. It should be noted here that no participants in the current study described any advice or management strategies to help reduce this sense of isolation.

Clinicians should be aware they too are potential causes for exacerbating the sense of isolation. A number of interview participants described clinical appointments when they raised the issue of PDN and the distress it was causing, to no avail (codes *HCP don't ask* and *Nobody is listening*). Participants described *Conveyor belt clinics* where there was no time or opportunity to raise issues that were pertinent to them. Clinicians need to be mindful of the opportunity they have to increase iatrogenic disability through the manner and conduct of their clinical appointments (Traeger *et al.*, 2015).

Research in communication around LBP has demonstrated the discrepancy between what clinicians say and what patients hear. Clinicians believe they provide clear information about a pathology or treatment, but the message heard by patients is understood to be much more concerning or worrying (Darlow *et al.*, 2012; Darlow and Dowell, 2013). Participants in the current study used phrases such as "…nerve damage…" when describing the causes of their PDN experience. These phrases are likely to derive from clinical appointments and suggest clear lines of causation from their diabetes, to the pain and disability they experience.

The impact PDN has on sleep quality is well documented (Zelman, Brandenburg and Gore, 2006; Alleman *et al.*, 2015), but the outcome measures routinely used in quantitative research (for example, MOS) may not be sufficiently sensitive to capture the fatigue impact of PDN. The participants in the current study identified the sense of fatigue they experienced through the day, as a separate issue to disturbed sleep. This fatigue had consequences for day-to-day life (*Fatigue with PDN*) and for people in their work role (*Struggle to get up for work*). The identification of fatigue as an issue in its own right has only been relatively recent. Research in rheumatoid arthritis found that people would rate fatigue as a significant functional impact on a daily basis, despite the objective markers of disease activity being stable and within appropriate limits (Hewlett *et al.*, 2005). Advice for fatigue and sleep management is now considered a core aspect of management for rheumatoid arthritis (Cramp *et al.*, 2013). No participant in this study had received any specific advice or management strategies that focussed on sleep quality or fatigue management.

The current study found a breadth of impact which is in-line with recently published results from another qualitative study that used mixed focus group and interview methods (Brod *et al.* 2015a). The study by Brod *et al.* (2015a) was conducted in the US with a more ethnically diverse sample (mainly Caucasian and Black American participants (86%)). Other sample variables are broadly similar to the current study. Brod *et al.* (2015a) identified four domains by which PDN impacted on the lives of their participants: physical function, daily life, social/psychological and sleep. Physical function included issues such as reduced exercise capacity, difficulty walking and fatigue. Daily life was affected at home by reduced enjoyment, and at work with reduced productivity. Participants described significant anxiety and limits to their social life. The majority had difficulty initiating or maintaining sleep. It is encouraging that the range of impacts presented by Brod *et al.* (2015a) and the current study, remain similar irrespective of the difference in ethnic sample diversity and health care systems experienced by USA and UK participants. This suggests some universality of the experience of PDN.

Brod et al. are working to develop an outcome measure that is based on the patient description of the impact of PDN (Brod *et al.*, 2015a). They feel this is important to allow healthcare interventions to be measured in a form based on the patient needs. The range of impacts experienced was not captured with sufficient accuracy by current outcome measures. Whilst development of an outcome measure is important, the current study has moved in a different direction, exploring participants' self-management strategies and their perspectives on pain management strategies as an intervention for PDN and associated impacts.

*4.9.2 The issues related to patient self-management of PDN*

Medication management is the mainstay of national and international guidelines for PDN (Bril *et al.*, 2011; NHS BNSSG, 2012; NICE, 2013a). There was a range of responses and approaches to medication. Some participants took no medication for PDN because the interference PDN caused did not warrant daily medication. Other participants had found a medication strategy that was effective and allowed them to maintain life activities with minimal interruption from PDN. Some participants gained benefit from medication, despite not taking the drug as it was prescribed. Others had not found medication effective; this was due either to minimal reduction in symptoms, or intolerable side effects. Although taking detailed drug history was not part of the interview schedule, this range of responses is broadly in line with the suggestion from Moore, Derry and Eccleston (2013) noted earlier, that there were subgroups of 'responders' and 'non-responders' to analgesic medication.

Participants began to feel abandoned once the medical teams ran out of medication options. From these interviews, participants felt abandoned for two reasons, firstly because

clinicians may not have allowed them an opportunity to describe the impacts of greatest importance. The structure or conduct of individuals' clinical appointments did not allow discussion of issues such as social isolation or sex life. A study into the experiences of women with long-term health conditions (18 of 25 with diabetes) explored the nature of the relationship patients had with clinicians (Fox and Chesla, 2008). Relationships were placed on a continuum from 'connected' to 'disconnected'. The connected relationships were characterized by respect and authentic empathy, whereas the disconnected relationships were characterized by the patient feeling treated as a diagnostic label, rather than a person. This treatment-as-diagnosis led to a sense of abandonment, which has been similarly identified in other chronic health conditions, including rheumatic diseases (Haugli, Strand and Finset, 2004), FMS (Åsbring and Närvänen, 2002), irritable bowel syndrome (Håkanson, Sahlberg-Blom and Ternestedt, 2010) and persistent LBP (Bunzli *et al.*, 2013; Snelgrove and Liossi, 2009).

Secondly, participants felt abandonment because there was no clear route forward for help to reduce or manage the impacts they experienced. Clinicians were seen as the source of advice and treatment for managing PDN and its impacts. The participants in the current study found there was little or no help forthcoming from clinicians once medication options were exhausted.

It is clear PDN is a multi-faceted condition requiring a multi-faceted approach to management, yet the majority of participants in this study received little or no guidance beyond medication. Only the participant who had attended PMPs for other pain conditions had received advice on sleep and psychological coping strategies.

Participants sought information to help them manage and cope with PDN from many sources including the Internet, newspaper advertisements and social media sites. Participants had experimented with a wide range of approaches to help themselves – usually with limited success. The experimentation with extreme techniques such as walking on stinging nettles, suggest being at the end of one's tether. Generally, participants had not been advised of other evidence-based strategies, that may have positive benefit.

*4.9.3 The issues related to physical activity*

As noted in the results, participants discussed physical activity and exercise synonymously. No participant in this study had been advised about specific exercise or activity to help with PDN. Their perspective on the role of physical activity in the management of PDN was only speculative. While a range of activity levels and attitudes to activity and exercise were present, it was clear participants would be very cautious with starting any form of physical activity that could potentially increase their pain. The competing perspectives articulated were that activity hurt too

much to be possible and, because PDN was due to nerve damage in the feet, there was no mechanism for exercise to alleviate the pain.

Participants who were more positive towards physical activity wanted advice from HCPs, rather than exercise professionals such as gym or exercise class instructors. They wanted the advice to come from someone who understood the pathologies of PDN and diabetes.

Physical activity is a key principle of diabetes management (Nagi and Gallen, 2010). NICE guidance NG28 for management of diabetes (NICE, 2015b) refers readers to their guidance on physical activity for adults (PH44) (NICE, 2013b). General benefits of physical activity include reduced development of T2DM, cardiovascular disease and many musculoskeletal problems, also an improvement in mood, stress management and overall measures of wellbeing.

Despite public health promotion campaigns, society as a whole has become less physically active (Townsend *et al.*, 2015). The reasons for reducing activity levels, and the current obesity rates are complex and this discussion does not deal with them in full. It will focus on one issue that is of relevance to PDN. The reasons for maintaining fitness through exercise and physical activity are often framed in terms of minimising the risk of chronic disease. By maintaining an optimum body mass and fitness levels an individual is less likely to develop T2DM, cardiovascular disease and some cancers. A systematic review of the effect exercise had on glycaemic control and body mass in people with diabetes found that while HbA1c levels were improved (7.65% exercise vs. 8.81% control, $p<0.001$), there was no change in body mass (83.02kg vs 82.48kg, $p=0.76$) (Boulé *et al.*, 2001). The study authors concluded that the improvement in HbA1c was likely to reduce the risk of diabetes complications. In clinical practice this research suggests people need to invest time and resources into exercise, with the expectation of not developing complications and seeing no or little change in body mass.

Chapter 2 presented the studies which were retrieved as part of a systematic review, they found that regular engagement in aerobic exercise did not improve pain related to PDN (Dixit, Maiya and Shastry, 2014), the statistical difference in outcome was due to the control arm worsening in pain scores. The practice of regular Tai Chi had positive effects on a quality of life measure (SF36) that included bodily pain scale, but the results from the Neuropathy Total Symptoms score were more cautious (Ahn and Song, 2012). What was consistent in these studies were that significant results arose because the control arms worsened across the data points, rather than the intervention arms improving. This was whether the outcome measure was SF36, Michigan Diabetic Neuropathy score, or the NeuroQOL instrument.

The research evidence does not currently indicate the effect that physical activity would have on pain in people with PDN. At best, physical activity might reduce the possible worsening of pain. Lack of improvement in pain may lead to the view that physical activity is a pointless pursuit and use of resources. It is possible the participants' perspectives that exercise would not be an effective approach may be true. Engagement in activity may offset worsening in other aspects of life quality but these data come from a few studies with methodological flaws and requires verification. At present, there is a lack of robust literature investigating different types and dosages of exercise that would allow clinicians to provide clear guidance to people with PDN.

*4.9.4 The issues related to psychological coping*

Some participants had exposure to psychological coping strategies and found these to be of benefit, but other participants were not willing to consider mood and psychological variables as relevant to their experience of PDN. When participants spoke about the causes of PDN there were strong Cartesian descriptions used, a clear separation between *mind*, as a location for mood and emotions, and *body* as a generative location for pain experience. Yet we know from a wealth of research that there are bidirectional interactions between mind and body (BPS, 2010; Kirkengen *et al.*, 2015). If mood states are an issue to the person with PDN, it maybe helpful for these to be acknowledged by the person and by any clinician they are in contact with. Acknowledgement of patient distress has been highlighted as good practice in the fields of oncology (Fallowfield *et al.*, 2001), palliative care (Lamont and Christakis, 2001) and primary care (Pincus *et al.*, 2013; Hasenbring and Pincus, 2014) as examples.

Having a long-term condition such as DM is associated with higher prevalence rates of depression than in populations who do not have these conditions (Baumeister, Hutter and Bengel, 2012). A cohort study of people with Type 1 and T2DM (n=1456) found 32% (CI 29.5-34.6%) experienced mild to severe anxiety, and 22.4% mild to severe depression (CI 20.2-24.7%). These results are higher compared to those reported in a recent study defining normative HADS data in UK adults (n=6280) in which moderate-to-severe anxiety was present in 12.5% of males and 19% of females, and moderate-to-severe depression in 6.9% of adults (equal in male and female respondents) (Breeman *et al.*, 2015).

It cannot be said that diabetes causes depression; there are risks of increased depression associated with lifestyle factors such as alcohol and tobacco consumption and the risk is reduced with higher socio-economic status and older age (Collins, Corcoran and Perry, 2009). Similarly, having persistent pain is also associated with an increased prevalence of depression (Campbell, Clauw and Keefe, 2003) and anxiety (de Vlieger, Crombez and Eccleston, 2006). It maybe

appropriate to consider that people with PDN have (at least) two health-related contributory reasons to experience depression.

The approach of a clinician can determine if patients are offered help to manage adverse mood states. An interview study with physiotherapists found some clinicians acknowledged patient's depression and anxiety, but did not recognise them as contributory to the presentation of LBP, or as variables modifiable through physiotherapy intervention (Synnott *et al.*, 2015). If clinicians do not recognise these mood states in patients, or place value on them for clinical intervention, then it is highly unlikely that any meaningful treatment plans will be instigated.

The management of mood states can involve passive and active approaches. Passive approaches include appropriate use of anti-depressant and/or anti-anxiolytic medication as identified by the patient and prescribing clinician. A recent Cochrane review of treatments for depression co-occurring with diabetes, found both psychological and pharmacological treatments were of benefit in the short to medium term. Only the prescription of anti-depressants was associated with a clinically meaningful reduction in HbA1c (Baumeister, Hutter and Bengel, 2012). The active treatment approaches for depression include moderate exercise, goal setting and increasing social contact. For anxiety a graded exposure approach to worrying situations can be appropriate. These same approaches are used for the multi-dimensional management of persistent pain (Leeuw *et al.*, 2008; Bair *et al.*, 2009).

The few participants who had attended multidisciplinary PMPs for other reasons, felt the strategies taught on those programmes, particularly relaxation techniques, were applicable to their experiences of PDN. The guidance provided by the British Pain Society on running PMPs highlight that potential participants cannot be coerced to attend a programme (BPS, 2013). The active engagement by the participant in the programme is vital as the strategies are active rather than passive. The rejection by a significant proportion of the interview participants suggests that, at present, psychological approaches would not be deemed appropriate by many people with PDN.

### *4.10 Limitations specific to the patient study*

#### *4.10.1 Interviews*

The primary limitation of this study was the lack of sociodemographic diversity in the sample population. All except one participant identified as White British. Different genetic profiles and ethnic backgrounds have differing prevalence rates for diabetes (Gujral *et al.*, 2013). These differences may affect the tendencies towards the underlying pathophysiology of PDN. Different social groups also have tendencies toward different pain coping strategies, for example African

American patients report using distraction and praying/hoping strategies for coping with pain, whereas Caucasians report greater use of ignoring and coping strategies (Edwards, Fillingim and Keefe, 2001; Hastie, Riley and Fillingim, 2004). The participants in Brod *et al.* (2015a), a qualitative study, had a greater variety of ethnic backgrounds, and the results of that study were in broad agreement with those presented here.

Interview participants were not asked about any religious beliefs or affiliations. The relationship between belief and pain coping appears complex. It appears some aspects of religion can be adaptive to supporting living with persistent pain, and other aspects may be maladaptive and be more associated with passive behaviours (Wachholtz, Pearce and Koenig, 2007).

As identified in Chapter 3, the philosophical position of qualitative research is that results do not aim to be generalizable beyond the context in which the original data were gathered. The results and conclusions of this study should be considered with the known lack of ethnic diversity, the unknown religious beliefs that existed in the population of participants, and the social context of the NHS system in the UK.

Lastly, the perspectives on physical activity and psychological coping reported by participants were essentially speculative. Although the PMP outline was used as a prompt for discussion few participants had actual experience of attending a multi-disciplinary pain programme.

*4.10.2 Questionnaire*

The aim of the complication questionnaire was to obtain a sense of how participants would prioritise the management of the diabetes related complications that they experienced. The imposition of a rating scale of 1=most interfering problem, 2=next most interfering etc. suggested that it was possible to clearly rank these problems and their management. In reality, participants were often unable to rank their problems in a clear sequential manner and this was not due to any fault on their part, but due to the inflexible nature of the rating scale.

The design of the questionnaire did not take into account the different considerations between complications that are on-going, such as the management of blood sugar levels, and the management of occasional complications, such as minor foot ulceration. Were this aspect of the study to be repeated, the questionnaire should be designed to take these different considerations into account.

*4.11 Conclusions*

The study has shown PDN has wide-ranging impacts on quality of life, beyond those found using quantitative questionnaire-based research designs. These impacts can be reduced when medication is successful, but there are people for whom medication options appear not to be successful. Participants had not been advised of other management strategies by clinicians. This left them with a sense of abandonment and resulted in them experimenting with uncommon management strategies. Some participants would be open to physical activity, but others saw no role for activity in improving their symptoms. Participants who had psychological coping advice for other persistent pain conditions felt these strategies were useful for PDN, but there was ambivalence from other participants, to these strategies.

Were a PDN-specific pain management programme to be available, it is unclear 1) given their perspectives on physical activity and psychological coping, whether patients would engage and, 2) whether clinicians who manage DM and PDN would feel such a programme was appropriate for their patients. The next chapter will present the perspectives from a range of clinical specialists on the appropriateness of these strategies for PDN.

The uncertainty from patient participants suggests more needs to be understood about their priorities for managing symptoms and impacts of PDN they experience. It maybe their main priorities could be matched to existing evidence based management strategies. Equally it maybe that patients' priorities cannot be matched to existing strategies and novel, innovative approaches are required. This question is the focus of Chapter 6.

# Chapter 5 – Results from the clinician interview study.

*Having described the perspective of people with PDN in the preceding chapter, Chapter 5 details results from the interview study with clinicians. Please refer back to Chapter 3 – Methodology and methods, for the details of the study conduct.*

## *5.1 Clinician results*

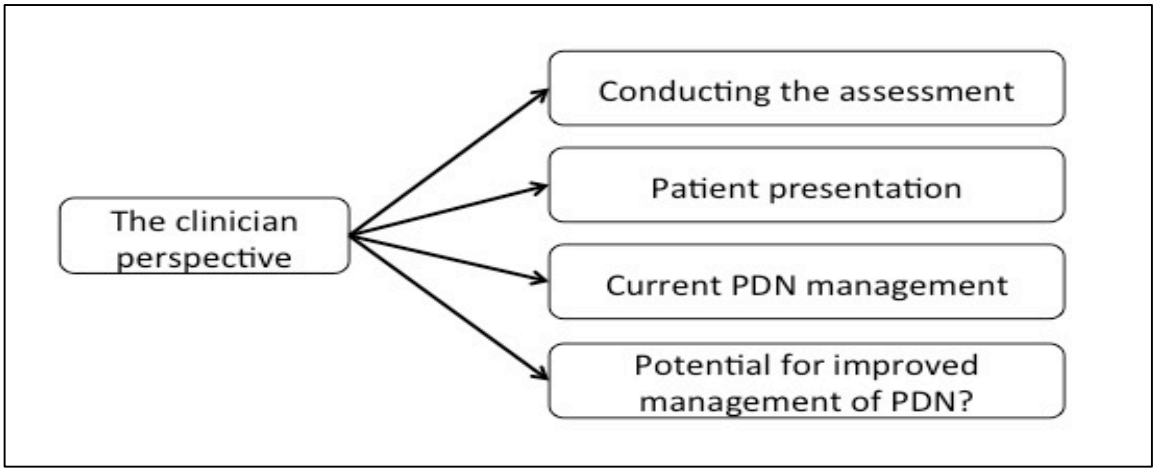
Eighteen HCPs were interviewed representing various disciplines (see Table 11). Sixteen of the clinicians were from secondary care organisations and two from primary care. Ten clinicians were considered specialists in diabetes management, six as specialists in pain management and the two clinicians from primary care as generalist clinicians. Interviews lasted 30-60 minutes.

Table 11 - Clinician professional role

| *Profession* | *N=* | *Diabetes* | *Pain* | *General* |
|---|---|---|---|---|
| ***Consultant diabetologist*** | 4 | 4 | | |
| ***Consultant anaesthetist*** | 3 | | 3 | |
| ***Secondary care podiatrist*** | 2 | 2 | | |
| ***Research nurse*** | 2 | 2 | | |
| ***Secondary care physiotherapist*** | 2 | | 2 | |
| ***Clinical psychologist*** | 1 | | 1 | |
| ***Research dietician*** | 1 | 1 | | |
| ***Secondary care diabetes specialist nurse*** | 1 | 1 | | |
| ***General practitioner*** | 1 | | | 1 |
| ***Primary care practice nurse*** | 1 | | | 1 |
| *Total* | **18** | **10** | **6** | **2** |

Results have been presented within superordinate themes created from the analysis (Figure 14). These superordinate themes have been laid out as a patient may journey through health services for help with PDN. Exemplar quotes have been used, identified by the clinician's profession. New codes were created up to the final interview, which suggested that a point of saturation, where all perspectives had been explored (Guest, 2006; Morse, 1995), was not reached in this study. It proved difficult to recruit clinicians from primary care; notably, the study did not interview podiatrists from primary care who may have different perspectives than their colleagues in secondary care.

Figure 14 - Overview of clinician themes




*5.2 Superordinate theme: Conducting the assessment*

Clinicians spoke about two aspects of communication through the assessment, one theme of communication issues on the part of the patient, and a second theme of communication issues they identified in their own practice.

*5.2.1 Theme: Patient communication issues*

Clinicians identified that patients may not raise symptoms of neuropathic pain during the consultation, even if they were experiencing them.

> *"I might see people a few times and then it comes up, that they've got painful feet or numb feet […] they haven't thought that it's something to bring [to the consultation]." Diabetes specialist nurse.*

> *"…other times you do have to ask because they don't think it's relevant for whatever reason even though its pain in their feet they say 'oh yeah well it keeps me up at night'." Podiatrist 2.*

Clinicians suggested patients were aware diabetes could cause sensory loss and numbness, but were less aware that pain could also be part of the presentation.

> *"…'Do you have painful neuropathy?' and the patient has gone 'no', do they understand what that sentence actually means, I strongly suspect not and that probably needs to be worded in a different way." Research Nurse 1.*

> *"The pain, I don't think particularly they do, numbness and gangrene, […] they're worried they're going to get gangrenous feet but I, perhaps they don't link it [pain] particularly." Practice Nurse.*

*"I don't think people mention to them the possibility of getting pain as a result of their neuropathy." Diabetes Consultant 4.*

Clinicians suggested it took time to build a therapeutic relationship. Some symptoms, such as erectile dysfunction, would not be raised at first consultation but at subsequent meetings once trust was established.

*"I think very often it is only once they feel comfortable with you, and they've built up that relationship, and they have had a little bit of education during the consultation." Research Nurse 1.*

*5.2.2 Theme: Clinician communication issues*

Clinicians identified that patients were not solely responsible for raising pain as an issue; and noted issues within their own clinical practice and communication skills. Some clinicians indicated that they were not routinely asking about pain symptoms.

*"Often these people will come in and unfortunately no one before will have asked them about any symptoms that they have around pain." Diabetes Consultant 2.*

*"We are trying to change, actually starting to ask people 'Are you in pain, do you have trouble sleeping, what is it one foot, both feet, how's it going?' and you start to drill down what actually is the problem." Podiatrist 1.*

*"I don't do often enough is to say, you know 'Are you getting any trouble with your feet?'" Diabetes Specialist Nurse.*

Clinicians noted they each had special interests; only when pain and associated pain management strategies were part of the individual clinicians' interests, were they likely to develop specific communication skills in these areas.

*"I think with all of these things, it is someone putting their head above the parapet and being really interested in it. [PDN] is their particular interest and develop the skills and expertise of managing those patients." Diabetes Consultant 3.*

*"I think that having a specialist service to go to is extremely important and part of that is the expertise and the knowing what other services are around and part of it is actually the fact that they really get listened to and the benefit of going where a specialist is really interested in all the details of this intractable problem." Diabetes Consultant 4.*

Organisational contexts were identified which could further reduce the likelihood of enquiring about pain. Within the diabetes multidisciplinary team individual clinicians described focussing on a specific aspect of patient management.

> *"Um, but generally, my role is about managing glucose levels." Diabetes Specialist Nurse.*

> *"We are very good at things like eye screening and any of the other microvascular complications, you know checking their kidneys, checking their eyes, however neuropathy maybe 'I've got some pains in my feet' sometimes that's overlooked." Research Dietician.*

In primary care the computer system consultation proforma did not include an opportunity to add pain symptoms.

> *"we talk about the pulses; do we talk about pain? No, we don't actually, there's nowhere to record it [on the proforma]. […] It's probably lost data actually." Practice Nurse.*

Other clinicians routinely considered pain in their consultation, or stated it was the patient's agenda, which was at the centre of the consultation.

> *"It depends on how you organise your clinical consultation, mine's usually 'Nice to see you, why are you here? What's on your agenda today?'" Diabetes Consultant 3.*

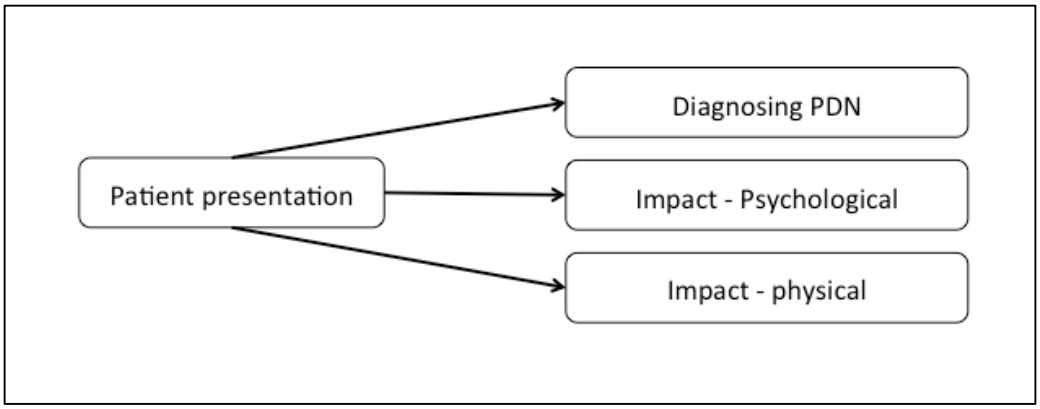
> *"As long as someone has a pain condition, it's always based on that individual assessment. […] because everyone is so different anyway, everyone has got different lives, different responsibilities, they've got different fears, views, different ways of coping, and again it's [assessment] really highlighting the main issues for that person." Physiotherapist 1.*

In summary, participants identified issues from both sides of the clinical encounter which contributed to PDN and its impacts not being raised. If PDN or its impacts were not raised they could not be dealt with or management strategies discussed.

### *5.3 Superordinate theme: The patient presentation*

This superordinate theme contained three themes: *Diagnosing PDN* described how clinicians arrived at a certain diagnosis for the patient's problem; *Impact - Psychological*, and *Impact - Physical*, described what clinicians noted in patients with PDN (Figure 15).

Figure 15 - Patient presentation




*5.3.1 Theme: Diagnosing PDN*

Clinicians from primary and secondary care, whether considered specialists or generalists, highlighted the difficulty of being certain in the diagnosis of PDN, rather than a differential diagnosis. Possible differential diagnoses included vascular pain, neuropathic pain from lumbar spine nerve root compression or spinal stenosis, and neuropathic pain from excessive alcohol, vitamin deficiency or other causes. They described using objective clinical assessment procedures (sensitivity assessment with monofilaments) or referral for tests by other departments (nerve conduction studies). All the clinicians stressed the most important aspect of their assessment was listening to the patient's subjective history. They were interested in the distribution of the symptoms, the words used to describe the symptoms, and the pattern across a day. The subjective narrative informed their objective assessment that confirmed or refuted a hypothesis of PDN.

> *"Right, so take a full history, and the first question I immediately ask myself 'Is this painful diabetic neuropathy, or have they got other causes for the pain?' The vast majority do indeed have it, very occasionally I see people where it is not clear or where they have a second cause for pain as well." Diabetes Consultant 1.*

> *"I want to exclude that there is something else going on, that it is not an ischaemic pain rather not a neuropathy, that it's neuropathic pain rather than an ischaemic pain." Diabetes Consultant 2.*

> *"or other kinds of things that can sometimes mimic it. Once I'm pretty clear with the diagnosis then we'd start trying treatments and follow the various protocols that are available for managing it, so starting off with something like amitriptyline." GP.*

When convinced that PDN was the patient's most appropriate diagnosis, clinicians identified a wide variety of impacts PDN had on the individual, both psychological and physical.

*5.3.2 Theme: Impact - Psychological*

This theme contained clinicians' reflections on how PDN affected patients' moods or cognitions. Most frequently, clinicians identified the patients as having some level of depression. Clinicians rarely used validated measures to screen for depression, but inferred the affected mood from the patient's language and behaviours and their own knowledge of chronic health conditions.

> *"a lot of them [patients] are of low mood, some can be irritable with family members, […] not that I'm a doctor or anything but they seem depressed to me." Podiatrist 2.*

> *"They've lost their jobs, their families are, you know, their relationships are in trouble, as I'm sure you're aware there is a huge incidence of anxiety and depression in pain patients." Pain Consultant 1.*

The specialist diabetes clinicians were interested in depression for the impact it had on management of diabetes. Self-motivation required to continually manage blood sugars could be negatively affected by depression. Positive coping behaviours might not be as frequent in the presence of low mood.

> *"I think what we try to do is, we know that people who have psychological and psychiatric comorbidities do not engage with treatments well and do much worse, we know that it has impact on their overall [blood glucose] control and compliance with medications […] we can treat them from the psychiatric and psychological comorbidities point of view in order to improve their micro- and macrovascular complications and hopefully in doing so have some impact on their overall health." Diabetes Consultant 2.*

Clinicians noted anxiety in patients. They described patients were worried about causes of pain, whether something more sinister had been missed, patients were often concerned about the unpredictable pattern of pain, and were concerned pain indicated possible, or further, amputation would be needed.

> *"They don't do things because they are worried it will trigger their pain." Diabetes Consultant 1.*

*"…which makes the pain appear worse, which makes the anxiety worse and so on. So if you can help reduce the anxiety that they're [in], it's not necessarily going to get any worse, it's not going to be, not necessarily serious, It's not a sign of cancer or something disastrous." GP.*

*"…you have people saying 'I had my leg off last year and a few weeks ago I noticed there was a problem with my foot but I didn't want to trouble you'." Podiatrist 1.*

Some clinicians described the emotional burden of guilt in some patients. They considered guilt arose because patients had been given advice and management strategies over the years that, for one reason or another, they had been unable to follow optimally and had therefore developed complications. These complications could include macrovascular and microvascular complications such as PDN.

*"I struggle a bit with this idea of fault and blame, and how with the one of the psychological themes with diabetic patients particularly those with complications are 'I'm getting my comeuppance, I should have as a child… if only as a teenager I hadn't…' all of that 'well I deserve it don't I because I've not controlled my sugars I've not looked after myself properly'." Psychologist.*

*"They reflect back on themselves and they think 'because I now have these problems it must be my fault I've not dealt with this very well, I am to blame'. So, they very much blame themselves, beat themselves up about it and have awful feelings of guilt and everything, which actually makes it incredibly difficult for them to look at managing." Research Nurse 1.*

Clinicians identified PDN had effects beyond the person who experienced it, to include their wider family and friends.

*"So family issues, pain can stop you from sleeping, it can make you grumpy, it can make you sad, it can impact all the interpersonal relationships with members of your family. So then you end up with marriage breakdown or not being able to feel that you're giving your children a good time, or your grandchildren. So yeah, it's much broader consequences than just the impact on yourself." Pain Consultant 2.*

*5.3.3 Theme: Impact - Physical*

Clinicians identified PDN had impacts on a wide range of day-to-day physical and functional capacities. The majority of clinicians commented on the impact PDN, and pain generally, had on

sleep quality. They noted the increased difficulty people had in coping with pain and life, if they have not slept well.

> *"I think it affects people a lot, um because of the pain, because of the sleep disturbance, so I think it is a miserable complication and of course diabetic complications cluster together. […] because you're not sleeping and you can't get away from it and you can't get it properly controlled." Diabetes Consultant 4.*

> *"I commonly hear people with painful neuropathy that sleeping sometimes is difficult because of the pain they are experiencing." Research Dietician.*

Clinicians described how patients were restricted in walking, both by PDN and also by diabetes and other related complications.

> *"Many of the patients I see are immobile because of their pain but also because of their other multiple co-morbidities with diabetes." Diabetes Consultant 1.*

> *"Well, from the diabetes perspective she was ah, a large lady and because of her neuropathy she wasn't very mobile." Pain Consultant 3.*

Clinicians were mindful of the way impacts connected with one another, for example being unable to work due to PDN could lead to reduced social life and sense of self-worth.

> *"Yeah, so if they can't work because of their diabetic pain, and then that means that they feel either they're isolated at home with their pain, because their work gave them a social side of things, or they feel worthless because they're not contributing to the family, or the family are in financial difficulty because they were the main breadwinner." Pain Consultant 2.*

The challenge of managing the unpredictable pattern of PDN was highlighted. The observation that PDN did not worsen in line with physical activity, but could have a 'mind of its own', meant it was difficult to gain control over the experience.

> *"Talking about base line setting, he [person with PDN in a PMP] was saying 'Actually this just isn't relevant for me, I've done all that', he was saying 'I've paced myself, it makes no difference, I can have a good day, I can have a bad day, it doesn't seem to relate to my activity very much'." Physiotherapist 2.*

> *"And my perception of diabetic pain is that it's not that their limbs don't, activity doesn't necessarily flare their pain up." Pain Consultant 2.*

Although clinicians were cognizant of the broad impacts PDN had both physically and psychologically, they stressed these impacts could not be disentangled from the psychological, physical and functional consequences of other diabetic complications. This made considering management strategies more challenging. Specialist diabetes clinicians including medical consultants, podiatrists and nurses, from both secondary and primary care were consistent in this view.

> *"I think so, the difficulty is sending some of these people to another appointment, which is a difficulty, when they are coming up here once or twice a week, they are seeing their GP, they are seeing their diabetes specialist nurse, they might be seeing their consultant, let alone having X-rays, their retinal screening, the numerous other appointments they have to attend anyway, they're not well people, trying to fit in something else a lot of them have kidney problems as well so are under the kidney specialist and seeing them regularly. It mounts up to an awful lot of appointments." Podiatrist 1.*

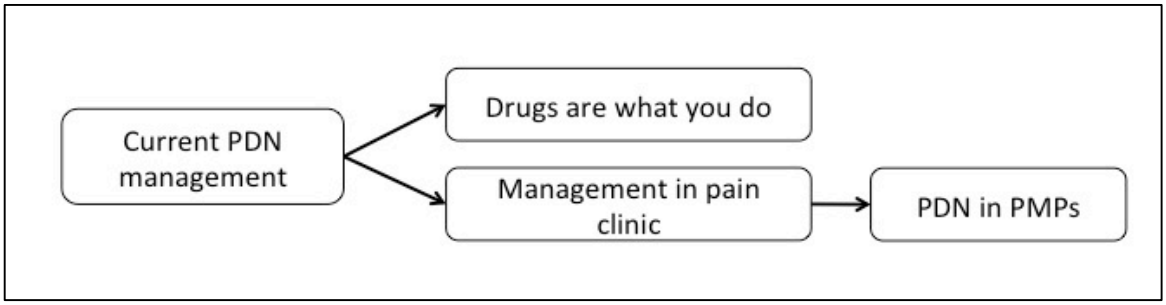
> *"I'm not the most unlucky person in the world to have eight different chronic diseases, actually this all stems from my diabetes." Research Nurse 1.*

To summarise section 5.3, all clinicians from primary and secondary care, whether generalists, diabetes or pain specialists, were familiar with the presentation of PDN. They were clear that people experienced significant amounts of pain with associated distress and functional impediment. The diabetes specialists recognised that PDN added further difficulties to the experience of living with, and managing diabetes as a long-term condition. They stressed that people with PDN were nearly always encumbered with other comorbidities due to their diabetes.

### *5.4 Superordinate theme: Current management of PDN*

This superordinate theme contained two themes: *Drugs are what you do*, and *Management in pain clinic*. This last theme contained a subtheme describing the clinicians' views of PDN in their PMPs, as they currently existed – *PDN in PMPs* (Figure 16).

Figure 16 - Current management of PDN




*5.4.1 Theme: Drugs are what you do*

In line with the evidence base, a strong theme from the clinicians was - *Drugs are what you do*. The clinicians most likely to be actively involved in managing people with PDN (GP, Practice nurse, DSN and Consultants) all described pharmacology as their initial strategy with the aim of reducing pain and subsequent impact.

*"I will say you need to see your GP, talk about duloxetine as being the recommended first approach and write to the GP to say." Diabetic Specialist Nurse.*

*"It would be a question of whether we initiate treatment for it and just see whether having Duloxetine or Amitriptyline or whether that actually makes, makes a difference to that pain." Practice Nurse.*

When clinicians consider medication, they were well aware of the evidence base and appropriate guidance documents.

*"So, at the moment the NICE guidelines and The British Pain Society all really say the same thing, there are only three drugs worth using Duloxetine, Pregabalin and Amitriptyline and the real question is in what order and in what combination?" Diabetes Consultant 1.*

*"I think we all play around with these various medications because they're useful but none is the panacea for painful peripheral neuropathy." Diabetes Consultant 3.*

Clinicians were clear their primary aim was to reduce the pain experienced and hence the related impact of PDN.

*"I mean that's our first responsibility as pain doctors is to try and reduce the intensity of the pain itself, because sometimes that's possible, sometimes it's not but, if it hadn't been tried then it needs to be tried." Pain Consultant 1.*

*"I also see my role as making sure that they have explored medicines as much as they want to explore them, accepting that most drugs we use for chronic pain are only about 30% effective." Pain Consultant 2.*

However, they were also aware side effects were a common issue and could limit successful analgesic management.

*"And so you'll get some patients, most patients have tried something, but a lot of patients have been bunged onto quite a high dose of an anti-neuropathic agent, which they've not got on with and they've failed with." Pain Consultant 2.*

*"if the patient doesn't take the amitriptyline because it sends them to sleep." Diabetes Consultant 4.*

Clinicians were cognizant that many medications prescribed for patients with PDN lacked efficacy. Consultants described the common scenario of patients who had been through multiple medications with no benefit.

*"We see that they have been through amitriptyline, duloxetine, Pregabalin, morphine, codeine and you name it. I often say to them that it looks like you've been through a lot of medications that may or may not have helped, and the patients often say 'Nothing helps'." Diabetes Consultant 2.*

*"Whereas there's others, and it's probably more common where whatever you do makes no difference whatsoever from an actual pain intensity point of view." Pain Consultant 1.*

This led to a situation and feeling of *Clinical Impotence*.

*"Um it's, well you know, 'you just have to put up with it', is the message and I give that message sometimes, […] I don't know what else to suggest." Diabetic Specialist Nurse.*

*"That's probably why we don't get more referrals with people with PDN because I imagine what happens is a lot of GPs and even diabetologists think that they've followed the guidelines. They've given the Gabapentin and whatever else there is and that hasn't worked so there's nothing that can be of any benefit for these people." Pain Consultant 1.*

*5.4.2 Theme: Management in pain clinic*

The second theme was *Management in Pain clinic*. There were perceived discrepancies between published prevalence rates of PDN in the wider community, and the relatively low frequency by which people with PDN were seen in pain clinic. Specialist clinicians in pain clinics and PMPs (Psychologist, Pain consultants and Physiotherapists), described seeing few, if any, patients with a primary diagnosis of PDN.

*"Yeah we do but surprisingly few given that it's so prevalent." Pain Consultant 1.*

*"We don't see a lot of people here with primary neuropathic pain, why might that be, particularly diabetic neuropathy, because it's common? If it's so common, why don't we see it in the pain clinic and why don't we see people further down the line in the pain management programme?" Physiotherapist 2.*

*"I don't suppose I've had anyone with type 2 with neuropathic pain." Psychologist.*

Referral routes to pain clinic were via the patient's GP, their secondary care diabetes clinicians and occasionally from a tertiary care PDN specialist clinic. Clinicians described the lack of structured approach to accessing specialist management; it was only assertive patients who got referred.

*"…only those people that shout the loudest, there's no overall global holistic view for this" Diabetes consultant 1.*

The pain consultants described their clinical consultation with people who have PDN as no different to those with any other person in pain. Their main aim was to listen to the patients' problems, to understand their clinical history and what interventions had been tried. They wanted to ensure that all possible conditions had been considered, so they could treat persistent pain appropriately, and not miss another condition that could be managed.

*"I don't think my approach to a diabetic patient would be any different to my approach to anybody that walks in. So I tend to do a consultation, it's a 45 minute consultation and I tend to get to an endpoint of offering them various different pain clinic options by a route of a conversation." Pain Consultant 2*

They felt their role was to rationalise the medication and to decrease the analgesia where there was little benefit to pain, or excessive side effects.

*"And then there's the group who are on quite a big cocktail [of drugs], who are not sure what they're on, and I might say 'Actually shall we just try taking one off, one*

*at a time and just see what happens?'. […] I guess to get rid of side effects they might be experiencing." Pain Consultant 2.*

Pain Consultants use injection therapy interventions for some pain conditions, but discounted these as inappropriate for PDN.

*"Yeah I mean nerve root block would be completely useless for diabetic peripheral neuropathy, I mean I guess you could conceive that an epidural might possibly be of some benefit, but as far as I'm aware there's absolutely no evidence for it." Pain Consultant 1.*

*5.4.2.1 Subtheme: PDN in PMPs*

This subtheme contained clinicians' views on whether PMPs as currently formulated were appropriate for PDN. Clinicians who delivered PMPs had two perspectives: 1) there were differences in PDN that needed considering and 2) the need for pain management should be based on the person not the pathology. These were speculative because, as mentioned, clinicians in PMPs had seen very few people with primary PDN referred to their services, and diabetes clinicians had little, if any, direct experience of the kinds of physical and psychological strategies deployed in PMPs.

*"I know very few people that have gone through [PMPs] with primary neuropathic pain and that's very interesting and I don't know why that is, but we don't seem to see them very much." Physiotherapist 2.*

Clinicians were aware neuropathic conditions were often spontaneous in pattern, rather than related to activity. They therefore questioned how relevant some strategies of PMPs were that focussed on activity patterns.

*"There is also a sense in which 'how can our exercise programme impact on that [PDN], when this pain is not particularly activity-induced?' So there is that other challenge now, from my perspective I understand that these nervy kind of unpleasant sort of neuropathic neuropathies can be impacted by stress levels, autonomic arousals, all those things." Psychologist.*

Similarly, one diabetes consultant felt most of the PMP strategies presented could be useful, but questioned how *Patterns of activity* (Appendix 6), could make much difference to a person's experience of PDN.

*"They're all [strategies] really relevant I would have thought - 'patterns of activity' I don't know how much difference that actually makes" Diabetes Consultant 4.*

In a counter viewpoint, clinicians considered the mechanism for someone's pain was immaterial, if they had persistent pain then many of the management strategies could be appropriate.

*"And I don't think there will be any difference between what kind of pain management programme would be useful for somebody with diabetic peripheral neuropathy, or any other type of neuropathic pain, I don't see their needs are any different from other patients who are in the pain management programme." Pain Consultant 1.*

*"But I also think that the impact on their lives is just as significant as somebody who's had a big accident, or they may, the reason they may see me is because they have diabetes but they also happen to have had something else stressful that's happened to them. So all those things that happen to a musculoskeletal patient could happen to a diabetic patient, like loss of earnings." Pain Consultant 2.*

Pain clinicians did not feel it appropriate to base treatment on a person's assumed pain physiology, as even pain that appeared related to tissue damage (nociceptive mechanism) would have increasing contributions from neuropathic and central pain mechanisms.

*"Whatever the original cause of that pain, whether it was purely a nociceptive cause like a back problem, they'd have had it for so long that it would have become neuropathic in nature because, you know, the pain will have become centralised which is by definition, I think anyway, neuropathic. So I don't think there's, erm, a great deal of difference." Pain Consultant 2.*

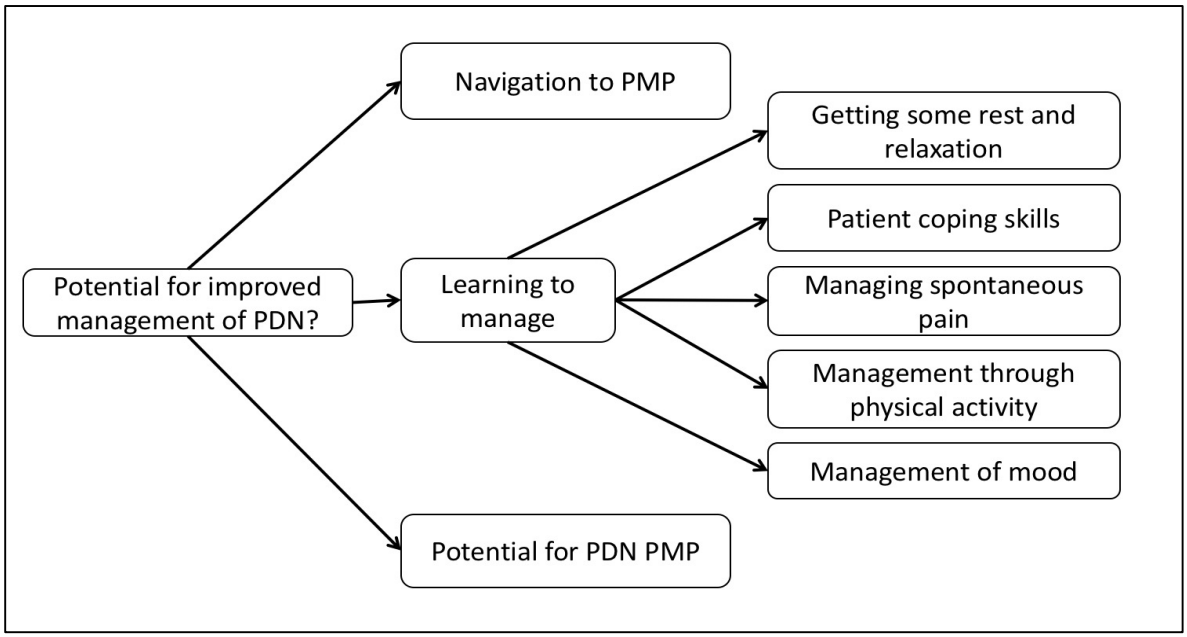
Overall, there were two perspectives from clinicians, 1) that people with PDN have some differences in presentation and hence need different consideration of management strategies, versus 2) pain and the impacts it has should be assessed individually and not dictated by diagnostic label. As this final quote from the Psychologist interviewed suggests, it was important to remember the person at the centre of the impacts, rather than the disease process:

*"I think the reason we don't get many for pain management with diabetic neuropathy [pause] is a fatalistic sense with the diabetologists that it's all part of your diabetes." Psychologist.*

*5.5 Superordinate theme: Potential for improved management of PDN?*

This superordinate theme (Figure 17) contained three themes: *Navigation to PMP* described how patients might find their way through the health service to PMPs; *Learning to Manage* described clinicians' perspectives on strategies they felt useful for managing and living with PDN. Lastly, clinicians' considerations for developing specific PMPs for PDN - *Potential for PDN PMP*. Theme *Learning to manage* contained five subthemes: *Getting some rest and relaxation; Patient coping skills; Managing spontaneous pain; Management through physical activity* and *Management of mood*.

Figure 17 - Potential for improved management of PDN?




*5.5.1 Theme: Navigation to PMP*

In order to access a PMP clinicians need to first consider this approach as a clinical option. Diabetes clinicians were not necessarily familiar with pain management approaches, or of the existence or relevance of their local PMPs.

*'Yeah, and after that [medication management] I don't know where to go." Diabetic Specialist Nurse 1.*

Others were aware of PMPs but had to refer the patient back to primary care and leave the decision on further management to the discretion of the GP. Local care pathways did not specify a point at which patients might be referred to a PMP.

*"I suppose it's not clear, I don't think, easily how we might access them [PMPs] referral pathways of ease to them it would be something to put on this integrated*

*care pathway [BNSSG DM management document] if there was a clear mandate to say 'yes, we'll take these patients'." Diabetes Consultant 3.*

Secondary care pain specialists highlighted navigation was not straightforward for patients or other clinicians in secondary care. They had rarely received referrals direct from diabetes clinics and acknowledged patients often had to be referred by primary care.

*"…a diabetic specialist wouldn't have direct access to our pain management programme, so they would have to go probably back to the GP and back in." Psychologist.*

*"I don't think I've ever had one from a diabetic clinic, I've only ever had them from GPs." Pain Consultant 4.*

Some pain clinicians highlighted exclusion criteria for PMPs often include progressive diseases. Clinicians raised the issue because PDN would fit this exclusion criterion if it were strictly applied.

*"One of these absolute criteria, the patient does not have malignant disease or progressive degenerative diseases such as ankylosing spondylitis or rheumatoid arthritis. And quite a lot of us, including me, have a slight, I slightly disagree with that, because you could put diabetics into that group as well, because it's a progressive disease." Pain Consultant 2.*

### *5.5.2 Theme: Leaning to manage*

This theme contained five subthemes. Each of these subthemes captured the clinicians' perspectives on wider strategies for managing PDN. Clinicians felt patients needed help to manage sleep and stress (*Getting some rest and relaxation*) and spontaneous symptoms (*Managing spontaneous pain*). They also felt that patients needed help to develop coping skills (*Patient coping skills*). Lastly, clinicians' perspectives of physical activity and psychological coping as strategies have been brought together in two subthemes - *Management through physical activity* and *Management of mood*.

#### *5.5.2.1 Subtheme: Getting some rest and relaxation*

When considering potential non-pharmacological management strategies, the inclusion of strategies to improve sleep and manage fatigue was felt vital.

*"You know strategies for sleep I probably would put that 1 or number 2, it is the thing that most of my patients complain about. […] a question I often ask patients is*

*'If I could wave a magic wand and get rid of one of your pains at any one time what would it be?' and they almost all universally say 'I'd like a better night's sleep'. So sleep is a big deal" Diabetes Consultant 1.*

*"…strategies for sleep would certainly be helpful because very often that is what keeps them awake at night […] you cannot manage when you're sleep deprived." Research Nurse 1.*

Clinicians were aware sleep and fatigue were not synonymous. They were aware fatigue could be an initial presenting symptom of diabetes, and fatigue was a potential warning sign of both hypo- and hyperglycaemic states.

*"Sometimes presenting with fatigue is one of the first things is the way people get diagnosed in the first place, so I think I would stuff something in there about fatigue management." Psychologist.*

They were aware of research and clinical approaches from other medical areas indicating fatigue management could be useful for their patients.

*"I think there's a lot of stuff that I've heard coming out of rheumatology is that the rheumatologists are, have been asking about symptom sets of people with rheumatoid pain. And actually, the thing that is the top of the list is not pain, it's fatigue." Pain Consultant 2.*

Clinicians were aware that stress further aggravated the impact of PDN on patients, stress could exacerbate the pain and pain itself was stressful. Responses to stress often incorporated choices of food, which may not be beneficial to overall diabetes management.

*"There is that other challenge now, from my perspective I understand that these nervy kinds of unpleasant sort of neuropathic neuropathies can be impacted by stress levels, autonomic arousals, all those things." Psychologist.*

*"I will certainly discuss with patients about stress management, in particular with type 2s' in relationship to food, I do a little bit of that work with them because very often people choose food to manage their stress." Research nurse 1.*

In order to manage stress, clinicians felt relaxation strategies such as breathing practice or mindfulness could be appropriate.

*"You know, if focusing on breathing can help, then in the middle of the night that might be a useful thing to do." Diabetic Specialist Nurse.*

*"I think for pain management, if you've got bandaged feet but you can still go onto a mat and do relaxation exercises." Pain Consultant 2.*

*"We do relaxation, we don't do a mindfulness-based programme, but we do use mindfulness based language sometimes, […] if that was on someone's flare-up plan as part of a way of managing a flare-up, that would be useful." Physiotherapist 1.*

Clinicians were aware of the complex interplay between pain symptoms, stress, lack of sleep, feeling fatigued, sensations of blood glucose level and management of diabetes generally. They were clear these interactions were not linear and that if one strategy did not succeed in helping the patient to cope, then other strategies needed to be explored.

*5.5.2.2 Subtheme: Managing spontaneous pain*

A hallmark of predominantly neuropathic pain from the literature and from the patient interviews was the unpredictable pattern of symptoms. Clinicians recognised this pattern could lead patients to avoid potentially aggravating pain but this had consequences for reducing activity and function.

*"I don't know how widespread, fear avoidance, fear of damage is for people with diabetic neuropathy, because I don't work with them I don't know how common it is, I wonder if that might be a difference. […] Yes. That there may almost be a value of saying well let's do non-weight bearing or reduced weight bearing exercise." Physiotherapist 2.*

Clinicians were aware PMPs tended to advocate pacing as a strategy to minimise aggravation of pain by activity, with the aim of giving control back to the person experiencing the pain. They suggested these strategies were less likely to be successful with spontaneous or paroxysmal pain.

*"But one of the things that pain management is sort of predicated on is that if you, stay within your limits and gradually work towards goals that things will improve and actually with that sort of ... paroxysmal pain then actually that sort of incremental benefit doesn't really accrue." Pain Consultant 3.*

Indeed, some clinicians who had experience of people with neuropathic pain on their PMPs reported that patients had told them pacing did not work.

*"he was saying "you know I've paced myself, it makes no difference, I can have a good day I can have a bad day it doesn't seem to relate to my activity very much." Physiotherapist 2.*

*5.5.2.3 Subtheme: Patient coping skills*

Clinicians felt potential clinical services needed to emphasize patient responsibility in managing their experience of PDN. They were aware that peoples' approaches to health responsibility varied.

*"…acknowledging and taking responsibility for their own health and choices, trouble is I see a lot of passengers" [here the clinician is referring to a patient who takes a passive approach to self-management, as opposed to active (a "driver")]. Diabetes Consultant 3.*

In addition to varying levels of responsibility, patient's ability to then self-manage health conditions could vary, dependent on intrinsic and extrinsic factors.

*"A lot of what we do is try to help people manage their condition and manage their lives more broadly, you know their condition is part of their life and their life impacts upon their condition, so quite often in general practice we accompany people through their journey." GP.*

'Acceptance' was often used; patients had to accept they had diabetes, they had to accept the need to make diet and lifestyle changes and accept the need to manage their PDN. Specialist pain clinicians raised acceptance as an on-going process, not a destination.

*"You do a lot of acceptance work with people with pain, they have to accept that they have a pain condition in order to build in strategies and it's very similar around diabetes. So, from that point of view it could be helpful, it could allow people to explore those difficulties." Physiotherapist 1.*

Some pain clinicians did identify possible differences between accepting diabetes, a clearly defined disease process, and accepting persistent pain, which is often considered a symptom of a pathology not yet diagnosed.

*"I suspect a lot of diabetic people, even if they haven't managed it very well, have had to accept they've got to live with it [DM] because it's not going to go away. Whereas a lot of pain patients are still looking for an answer. […] The problem, and I wonder if the diabetic people are probably better at acceptance because they know*

*what they've got [DM], whereas a chronic widespread pain condition is quite hard to get people to accept." Pain Consultant 2.*

Support from other people was considered vital for effective self-management. Clinicians suggested that people with PDN often felt isolated, both physically due to mobility restrictions and emotionally knowing no one else with similar problems.

*"I am sure it would be beneficial, it [PDN] can be incredibly isolating and the kind of people who get it tend to feel they are very isolated anyway, they are often the older people." Diabetes Consultant 4.*

The clinicians' awareness of patient's isolation and possible lack of support reflect similar themes identified in the patient interviews. Support to mitigate isolation could come from family and friends.

*"I mean if you were managing all of this without any support at home then that's hard too isn't it […] it's actually thinking well friendship supports or family supports maybe that's important." Practice nurse.*

*"the ones [patients] who do better are the ones who have family and support, the ones who don't do very well are the ones who don't want to engage at all, so they don't have any family or support." Podiatrist 1.*

Clinicians shared the view of participants in the patient interviews, that peer-support from other people with PDN was possibly viewed as more trustworthy than advice from professionals with no personal experience.

*"Which may actually work better is somebody with diabetes who's had experience of the whole of the condition and all that that entails, managing their diet, managing injections for example, dealing with those tussles between do I eat a bit more, what's the impact of that and all of that psychological challenge. Am I good, am I bad, who is in charge is it the diabetes, or is it me?" Physiotherapist 2.*

*"It's better that they hear from other patients rather than professionals [laughs]" Research nurse 1.*

*5.5.2.4 Subtheme: Management through physical activity*

All clinicians interviewed considered increasing physical activity levels would be useful for a multitude of reasons. They identified that patients often left the house less frequently than before PDN, had reduced specific physical activity and had fewer social engagements that

included physical activity. They had often become less physically fit. These changes to activity level made overall diabetes management more complicated. The loss of fitness could further impact on other complications and co-morbidities the patient experienced.

> *"But that said I certainly think that some form of physical rehabilitation is important, a lot of the patients I see tend to become more and more constricted and more and more house bound because they don't do things because they are worried it will trigger their pain." Diabetes Consultant 1.*

> *"Somebody's got cardiovascular problems because of their diabetes, like angina, and they can't exercise, and actually part of their, part of pain management is trying to get some sort of physical activity, that would be a barrier, but that would be the same for a lot of our patients." Pain Consultant 2.*

Clinicians recognised being more physically active and increasing the variety of day-to-day activities patients could then engage in, would likely benefit the person's mood state. This would have the additional benefit of reducing the focus on pain, by introducing distraction through engagement and occupation.

> *"That by exercising alright won't do them any harm, in fact it may well do them good both physically and psychologically, so empowering people to live normal lives." GP.*

> *"Just doing something can actually improve your mood and make you feel as though you've achieved doing something because these patients very often feel 'I definitely cannot do it', 'I cannot do it because of the pain', and whereas if you say have you tried this and they can actually do something it might make them feel like of 'oh, that's really good actually'". Research Nurse 1.*

Some clinicians specifically felt exercise would increase blood supply to areas of the body where it was compromised due to cardiovascular disease. They also identified the release of endogenous opioids caused by moderate exercise could improve overall sense of wellbeing.

> *"It's very difficult to get them out [being more active] which would be helpful because it would help their circulation, their whole being." Podiatrist 1.*

> *"Exactly, endorphins after exercise and feeling better about themselves." Research Nurse 2.*

Although clinicians identified potential benefits of increasing physical activity, diabetes clinicians expressed specific cautions. The medical consultants stressed diabetes affected many physiological systems, which led to more complex medical presentations than maybe usual in PMPs.

> *"I think physical activity has to be very carefully thought out, it would be unwise to say to them 'get out on a bike', might be alternative ways like swimming". Diabetes Consultant 2.*

> *"So I think it's about context and saying 'What do we genuinely think we can get the patient back to?' in other words, 'What degree of their immobility or lack of physical activity is directly due to the pain as compared to their other co-morbidities?'" Diabetes Consultant 1.*

Diabetes clinicians were specifically concerned about the risks increasing physical activity could pose to someone with insensate feet. They worried patients might be encouraged to increase activity levels without being reminded of the need for due care of their feet and checking footwear was appropriate to avoid ulceration. It should be noted that none of the diabetes clinicians had any direct experience of observing PMPs being delivered.

> *"I think one just has to be a bit circumspect in pushing activity, because I've seen in other areas of diabetic neuropathy people inadvertently say 'well, you need to do more' and then the patients come with foot damage because of following recommendations and doing more but damaging their skin and then ending up with problems." Diabetes Consultant 3.*

> *"I think that's a great idea, my only concern with our patients is that most of them don't have any protective sensation, so they are at massive risk of ulceration." Podiatrist 2.*

Diabetes clinicians questioned the difficulties present for patients to engage with the increasing their physical activity. These difficulties included the interactions present between activity levels, mood state, obesity and others in society.

> *"Sometimes their willingness to accept it because when people are very depressed all they want to do is cocoon themselves somewhere rather than necessarily go to the gym with their BMI of 50 and expose themselves to strangers, so is lots of other issues around why people do not want to be active". Diabetes Consultant 2.*

They felt it also depended on whether patients were adept at self-managing their condition and the complications that may come with it.

> *"…not easily, not easily, I think sometimes it depends whether they are a passenger or a driver." Diabetes Consultant 3.*

In contrast, the clinicians who were actively involved in PMPs (physiotherapists and psychologist) or referred to such programmes (pain consultants) did not share the concerns about the risks of increasing a person's activity level. Physiotherapists described how physical activity was introduced and used in PMPs. They described how each person was individually assessed to find a baseline for each of the exercises. These exercises were functional; they aimed to replicate some part of daily movement. The overall aim was to gradually increase physical capacity.

> *"Absolutely completely and utterly that's the basis of it, it's not random shoulder exercises and they're not aimed at curing anything, they're aimed at improving overall activation, reversing deconditioning that has happened." Psychologist.*

> *"…they can be modified as well, so I suppose the bottom line is, you know, even if it's difficult you can always do a small amount of one or you can do it in a different way, so there's always a way of developing that exercise programmes." Physiotherapist 1.*

Focussing on the risks specific to insensate feet, these clinicians felt they were aware of the dangers and the assessment required to optimise safety. They considered the activity component of PMPs could be adapted to the needs of this population.

> *"In fact, the exercises are no different than daily functional tasks, […] it's all part of our normal movement, so in terms of the worry about damage, that wouldn't be a worry that I'd necessarily have. Obviously, if people had open ulcers …" Physiotherapist 1.*

> *"Is one form of exercise more useful than another, but if they're saying I have problems weight bearing is it actually helpful to see that at face value and say 'okay let's do some non-weight bearing exercise' in a way that we just wouldn't do in a pain management programme." Physiotherapist 2.*

Clinicians were also cognizant of the need to check footwear was appropriate and check feet before and after any form of exercise. They were aware patients were taught and reminded of these checks frequently by diabetic specialist clinicians and felt strongly these checks were

integral to the patients' responsibilities for managing their diabetes. These checks were considered part of the patient's self-management.

> *"…they've been told all the time that they've got to look after their feet because they might be numb and that they've got to prevent themselves getting foot ulceration and things" Diabetes Consultant 4.*

> *"It would be perfectly reasonable to encourage, as part of self-care that people should [check their feet], but whether it's before they do specific exercise or whether it is part of what they do every morning, I would have thought it is part of what you should be doing every morning?" Psychologist.*

*5.5.2.5 Subtheme: Management of mood*

As highlighted in Section 5.3, clinicians were aware PDN was associated with worsening depression and anxiety states. Clinicians from both diabetes and pain specialities, and from primary care considered psychological support would have a beneficial role with people who have PDN.

> *"But psychologically there's definitely a need for them, just as there is for any patient who's struggling to cope with their pain." Pain Consultant 2.*

> *"Of course it's really important to look at the psychological aspects because two people can have apparently the same pathological or an anatomical problem." GP.*

One consultant compared the difference between staffing in adult and paediatric diabetes clinics. The inclusion of clinical psychologist support was common, if not universal, in paediatric and adolescent clinics. Other than the stress of managing a long-term health condition at a young age, this was a time when young people with diabetes were least likely to have additional complications to deal with. Once in adult clinics the access to psychological support becomes much more restricted and difficult to access.

> *"I think what we are lacking for not just here but nationally is a good and robust service that will offer psychological help to people in chronic disease in general and diabetes in particular. It's funny though you would not find a paediatric hospital where there isn't a clinical psychologist on the team for patients with diabetes." Diabetes Consultant 2.*

Clinicians described improvement in depression could lead to subsequent improvement in function, quality of life and overall diabetes management.

*"It gives me a better understanding if I know something about their depression, how they're going to be able to self-manage and make any changes. It's no point to ask a patient to make any changes if they're not in the right place and not able to do so." Research nurse 1.*

*"and a lot of people suffer with depression with their diabetes as well I'd say the majority of patients they come to us and they are depressed and comfort eat, adds onto weight." Research nurse 2.*

Goal setting was highlighted as important by physiotherapists. Physiotherapists would often use individualised goal setting with patients to help them achieve something and so manage depression.

*"So moving into a cognitive behaviour approach was more rehabilitation based was more goal focussed which isn't directly about the experience it's about moving forwards with life." Physiotherapist 2.*

*5.5.3 Theme: Potential for PDN Pain management programmes*

Clinicians provided some considerations for how PDN-specific PMPs might be used or fit into the existing clinical pathways. It should be highlighted these were suppositions, as they had no experience of such a programme specifically for people with PDN.

Overall, there were positive opinions that PMPs could be useful in helping people to cope better with the impacts of PDN.

*"I think everything [strategies] on there would actually be really useful." Research nurse 1.*

*"All of them [strategies] are relevant every single one of them" Podiatrist 1.*

Clinicians did not feel a programme could replace drug therapy, but it could be used alongside medication.

*"I think probably I mean you wouldn't want it after, because it will help you cope with what the drugs can achieve, and I don't think it would probably be a substitute for the drugs…" Diabetes Consultant 4.*

They did feel a programme more likely to be effective if delivered earlier, rather than later, in the development of PDN.

*"I sometimes think that the people we get here it's almost too late for some of these things, they are kind of too far gone to have effective interaction with, in terms of psychology.' Podiatrist 2.*

They considered a potential programme would not be necessary for everyone, but targeted to those people who were struggling to cope with their pain, its impacts and other events that were on-going in their life.

*"I would say probably glove and stocking distribution pain, neuropathic pain, but with quite a lot of lacking, so they're lacking in coping mechanism. So, they'll have other baggage around that, it'll either be, you know, it's usually a combination of factors, it's either financial difficulties and family difficulties, or anger management difficulties or things which are allowing them to now, which are not enabling them to cope with their pain. So, levels of distress that are high, not, so it's not likely to just be diabetes and pain, there's likely to be other things going on." Pain Consultant 2.*

It should also be considered whether the person was at a point where they were ready to make behavioural changes for PDN management. These patient perspectives can change, and on-going reassessment maybe required.

*"Some patients if you just suggest to them that what they would benefit from is a pain management programme when you first meet them you will just fail because they won't ... they're not ready to accept that." Pain Consultant 2.*

*"Some patients go 'oh, I don't think I like the sound of that [PMP], that's not for me, I want a treatment for my pain', many of them are far more pragmatic and reasonable, particularly once they have seen me in clinic a number of times and they know I'm at the end of the road." Diabetes Consultant 1.*

### *5.6 Discussion*

A range of secondary care clinicians who were specialists in diabetes and pain management, and clinicians from primary care were interviewed for this study. All clinicians were aware of the variety of impacts living with PDN can have on peoples' lives. The primary strategy identified was prescription of analgesic medications, or referral to a clinician who could prescribe. When these medications failed, there was uncertainty around alternative management strategies. Pain specialist clinicians felt that PMPs could be adapted to the specific needs of people with PDN.

When considering the applicability of PMP strategies to PDN, there were differing perspectives between groups of specialist clinicians, which will be explored in this discussion.

### *5.6.1 Clinical impotence*

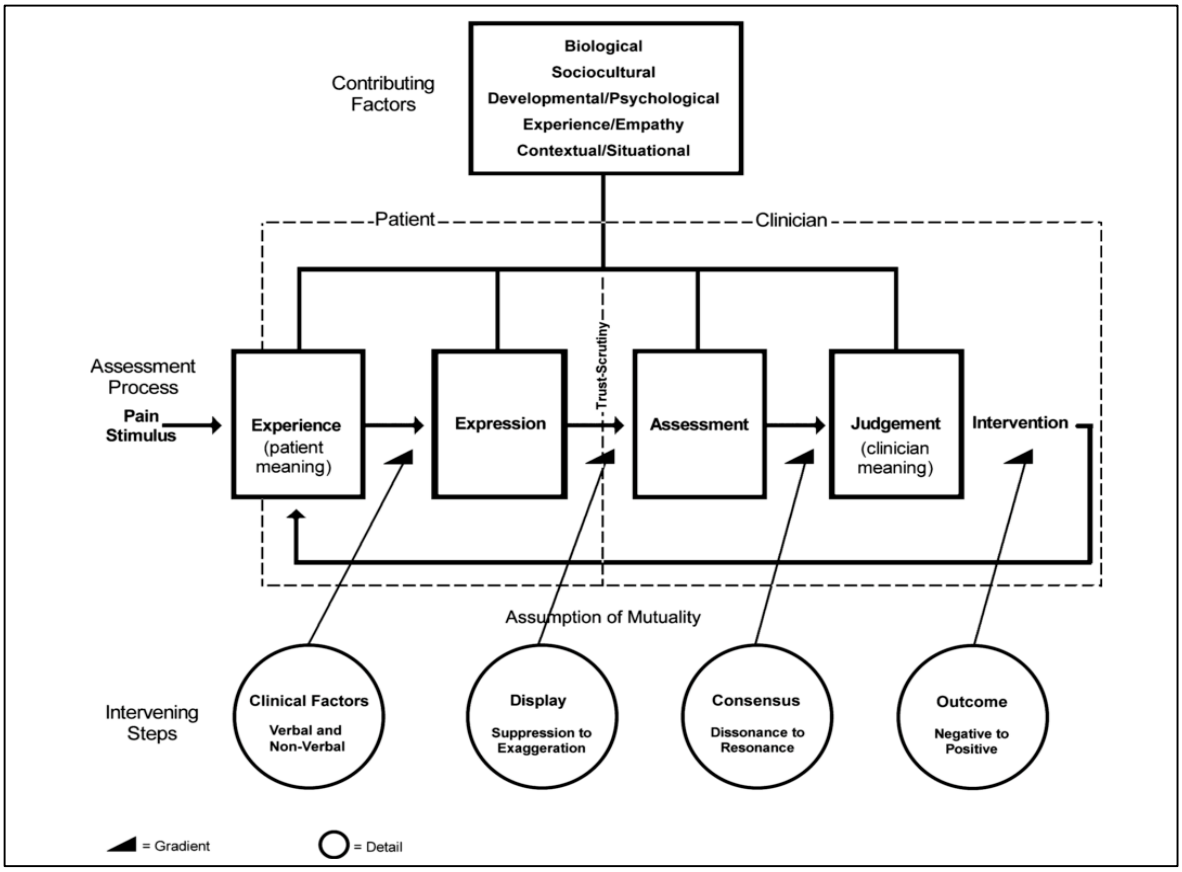
Some clinicians identified they did not ask sufficiently probing questions around PDN symptoms. This was usually either because the clinical focus of their consultations was another facet of diabetes management, or they knew the patient had PDN, but had exhausted all medication options and so did not ask because they had no alternative management strategies.

This issue may not be specific to PDN as there have been calls in medicine for improved consistency and depth of pain assessments (Ballantyne and Sullivan, 2015). As persistent pain of many causes has become more prevalent and increasingly costly to the person, health care systems and society, clinicians have been advised to consider pain as the fifth vital sign, along with blood pressure, temperature, heart and breathing rate (Gatchel *et al.*, 2007; Ballantyne and Sullivan, 2015). Guidance suggested better measurement would lead to better management, and self-report scales (NRS or VAS) were the most appropriate assessment tools (Schiavenato and Craig, 2010). A reduction of self-reported pain severity then becomes the aim of treatment. Researchers now suggest however that reliance on self-report scales is not appropriate as they not sufficiently nuanced to allow the patient to communicate their experience (Schiavenato and Craig, 2010). Ballantyne and Sullivan (2015), in their recent editorial, highlight the meaning patients attribute to pain, including the sense of helplessness and hopelessness can have large impacts on peoples' lives. These features of peoples' experience of living with pain related to PDN, and the issue with questionnaire-based research, have been explored in Chapter 4.

Pain assessments are complex interactions; researchers have advanced a model of the clinical encounter that allows considering the ways through which thorough assessment of PDN could succeed or fail (Schiavenato and Craig, 2010). The model (Figure 18) highlighted that patients must attribute meaning to their experience, and this meaning differs with social and cultural context; this has clear concordance with the MOM and Neuromatrix models outlined in Chapter 1 (Gifford, 1998b; Melzack, 2001). Patients have to express their experience by means of verbal, facial and non-verbal communication cues. The clinician needs to assess and interpret these cues prior to making clinical judgements.

To this point, Schiavenato and Craig (2010) describe the process as 'communication-as-interaction', two participants in a clinical relationship gaining an understanding of the problem. They term the next step where an intervention or treatment occurs as 'communication-as-transaction'.

Figure 18 - Pain assessment as a transaction, from Schiavenato and Craig (2010), (*reproduced with permission)*




The model shown above contains a number of features relevant to the current clinician interview study. The vertical line *Trust-Security* highlights the balance between patient's expression of pain by non-verbal and verbal means and the clinician's assessment. Individual clinicians are on a spectrum between an empathic and sceptical stance; if a patient believes a clinician to be sceptical of their experience, they may increase their pain expression in order to emphasise their need for treatment. If a patient is stoical to their pain experience, the clinician may conclude treatment of pain is not indicated. The decision by the clinician to treat or not to treat pain, and how concordant that decision is with the patient's expectations, is the transaction in question. This description of clinical relationships has resonance to the spectrum between 'connected' and 'disconnected' (Fox and Chesla, 2008), that were described in Chapter 4, section 4.9.2.

*'Assumption of mutuality'* describes the assumption that patients seek healthcare to reduce pain, and clinicians feel moral and ethical imperatives to reduce pain. If the clinical pain assessment is biased toward only using pain self-report measures because expectation of pain reduction is assumed and so must be measured, the patient may not be allowed the opportunity

to disclose the impacts they truly would want help to reduce. If clinicians assume patients are seeking pain reduction, yet feel they have no viable treatment options, the dissonance between their moral/ethical drive and their clinical treatment options may cause them to divert away from opening discussions around the patient's PDN (Schiavenato and Craig, 2010).

Within their paper Schiavenato and Craig (2010) suggest one reason why clinicians do not hear the patient narrative to be: *incompetence or poor clinical knowledge/skills* (Table 1, pg670). The diabetes specialist clinicians interviewed in this study did not appear incompetent, but some felt clinically impotent because, beyond medication, they had no management strategies to offer patients with PDN. The clinicians in this study were experienced in their respective professions. Having reached a level of expertise, the organisational culture clinicians worked in may not have permitted them to admit there were deficits in their knowledge, or it maybe they were not aware of what they did not know.

### *5.6.2 Differing concern about physical activity*

The diabetes clinicians interviewed had specific concerns about increasing the level of physical activity in people who had insensate feet. They were concerned that without appropriate foot checks for patients and training for clinicians, tissue breakdown may occur, leading to ulceration and potential amputation. The pain clinicians were aware of the risk to insensate feet and the need to check feet regularly; they felt exercise could be individualised appropriately to patients with PDN.

The perspectives of clinicians likely reflect their clinical experience. Podiatrists in secondary care were managing people who had critical tissue damage potentially requiring amputation. This interview study did not succeed in recruiting podiatrists from primary care who have a greater role in monitoring people in their caseload, rather than actively treating ulceration. Pain clinicians are not exposed to people with ulceration in the same way as podiatrists.

Given the known risk, it is surprising not all studies investigating physical activity in the diabetic population routinely record or report adverse events related to ulceration or skin lesions. For example Dixit, Maiya and Shastry (2014) investigating aerobic exercise highlight considerations were made to foot care and hypoglycaemia during and after exercise, but made no comment on whether the participants experienced any foot injuries due to the exercise(Dixit, Maiya and Shastry, 2014). Toth *et al.* (2012) and Kluding *et al.* (2012) reported adverse events related to hypoglycaemia and pain but none related to foot damage; Yoo *et al.* (2015) did not report on adverse events.

A recent non-systematic review highlighted specific considerations for prescription of exercise in patients with neuropathy (Colberg and Vinik, 2014). Advice included: regular foot checks and appropriate footwear, 'mild to moderate' intensity weight bearing exercise (both aerobic and resistance based), low impact exercise (water walking, hydrotherapy, chair based exercise), non-weight bearing exercise if current foot ulceration were present and inclusion of balance challenge exercise to mitigate the risk of falling. Colberg and Vinik (2014) do not define what they mean by 'mild to moderate' intensity activity. Moderate activity has been defined as an intensity when talking in sentences becomes difficult, and is recommended as the required intensity of activity to reduce the risk of many chronic health conditions (NICE, 2013b; Townsend *et al.*, 2015; WHO, 2017; Sparling *et al.*, 2015). This guidance for activity is generic and does not take into account other risk factors such as potential to ulcerate.

There appears a need for better consistency in reporting adverse events related to foot tissue damage in studies of physical activity in the diabetic neuropathy population. Currently clinicians are caught between appropriate caution to avoid injury and amputation and wanting to encourage people to increase physical activity for the associated physical and mental health benefits.

### *5.6.3 Treating the condition or treating the person?*

The diabetes specialist clinicians were well aware that people with PDN had coexistent psychological and social issues. There was lack of concordance between the widespread impacts identified, and the single modality management strategy, medication, which tended to be employed. These clinicians were well aware of the guidance for PDN and neuropathic pain management, from local, national and international sources. Reflecting on the language used, it could be suggested that they considered treating the *condition* of PDN.

National and international guidelines for pharmacology are similar but not completely concordant recommendations (Bril *et al.*, 2011; Spallone, 2012; NICE, 2013a). The details of these pharmacological recommendations can be found in Chapter 1, section 1.3. These guidance documents are focussed on treating the condition of PDN, rather than the person with the condition.

The language used by pain specialists that were interviewed focussed on the individual needs of the *person* who they assessed in clinic. They felt the person's diagnostic label to be less important than what impacts, due to pain, that person was experiencing. They then considered, in conjunction with the person, whether these impacts could be mitigated by strategies taught in PMPs, and whether the person was engaged with the ethos and aims of the programme.

This difference in treatment approach between diabetes and pain clinicians reflects a wider debate about pain. Diabetes is considered a disease in its own right. Whether T1 or T2, patients understand diabetes to be a diagnosis based on their presenting symptoms. Persistent pain in comparison has, for millennia, been considered a symptom of some underlying pathology that has yet to be diagnosed. Only in the more recent age of neuroimaging has pain been reconsidered as having the hallmarks of a disease process (Tracey and Bushnell, 2009). In the absence of other explanatory causes, persistent pain is now considered a diagnosis. If pain is considered a long-term disease with no curative treatment options available, then management of pain becomes philosophically more in-line with management of other long-term diseases, such as diabetes.

There have been similar developments in the approach to management of LBP. Guidance has developed from focussing on LBP as pathology, to using stratification tools that aim to individualise management packages. The STarTBack questionnaire is based on variables that are both known to affect the prognosis for acute LBP developing into a persistent pain problem, and are modifiable by treatment (Hay *et al.*, 2008; Main *et al.*, 2012). Rather than treating all people with LBP as a homogenous group, these questions allow a person's specific attitudes and fears to be assessed and then addressed, if required.

Helping diabetes specialist clinicians to consider the person with PDN individually, rather than as a diagnostic label, would facilitate the consideration of management strategies other than medication and reduce the feeling of clinical impotence. There are however two considerations; firstly, the literature reviewed in Chapter 2 demonstrated a paucity of research exploring the utility of pain management strategies in PDN. There is a need for further research investigating how these strategies may need to be adapted to be appropriate and acceptable to people with PDN. Secondly, diabetes clinicians identified people with diabetes as medically complex with multiple issues that may affect their ability to engage with physical rehabilitation and other pain management strategies.

### *5.7 Limitations specific to the clinician study*

Gaining access to interview clinicians proved difficult. All clinicians had very busy diaries and a number of potential interview participants declined the invitation to participate due to time pressures. There were participants from secondary care clinics representing two NHS trusts, but some were from the same team. This may have led to underlying team philosophies being represented in the interviews. For example, had podiatrists been recruited from different organisations, there may have been more variety in the perspectives of that profession.

Professions such as podiatrists and physiotherapists work in both primary and secondary care roles. This study only recruited representatives of these professions from secondary care. It is possible the perspectives of podiatrists in secondary care diabetes foot clinics, where the focus is on healing ulcerated areas of the foot to avoid amputation, may differ to their colleagues who work in primary care. The focus in primary care would be on regular monitoring rather than dealing with clinical crises.

Clinicians from primary care were recruited through advert in the Primary Care Research Network bulletin. This may have led to only research active or interested clinicians being aware of the study. This process also meant primary care clinicians were recruited and interviewed last. The interviews with secondary care clinicians were chronologically earlier in the study, allowing questions raised by one interview to be checked in subsequent interviews, this was not possible with primary care clinicians.

### *5.8 Conclusions*

Diabetes specialist and primary care clinicians were aware of the multi-faceted impacts PDN had on peoples' lives. Their primary management option was evidence-based medication strategies, which were not always successful. Once these were exhausted they had few alternative management strategies to offer and could feel clinically impotent.

Pain specialist clinicians felt strategies they currently employed for persistent pain of other causes could be beneficial but may need adaptation (approaches to physical exercise) or selection (acceptance rather than pacing). Their focus was on the person with pain rather than the diagnostic label.

The risk diabetes clinicians, particularly podiatrists voiced, regarding damage from increasing exercise load on insensate feet is important to recognise. Pain specialists were aware of the need for regular foot checks, a conservative approach to exercise load and alternative types of exercise. Further research is required to develop the evidence base for activity prescription with best ratio of risk to benefit.

People with PDN may be more medically complex than the majority of patients that are referred to PMPs, due to multiple diabetes-related comorbidities. These comorbidities are interconnected and need considering were a PDN specific PMP to be designed. Other than this consideration, there were no *a priori* reasons given by clinicians in this study for not further investigating the appropriateness of pain management strategies for people with PDN.

*The previous two chapters have outlined the findings of two interview studies. Some patients interviewed were sceptical that PMP strategies were applicable to the impacts of PDN they experienced. Clinicians felt that many of the strategies maybe helpful but highlighted that people with PDN were more medically complex than usual participants in PMPs and that care was required particularly with regard to physical activity.*

*The next chapter will describe the conduct of an Internet survey that asked people with PDN to highlight which impacts of PDN they most prioritised for better management. The impacts presented in the survey were based on the findings from the patient interview study (Chapter 4).*

# Chapter 6 – An Internet survey investigating the impact of Painful Diabetic Neuropathy (PDN) and patient treatment priorities.

*Chapter 4 described the results of an interview study with people who experience PDN. The results highlighted the impacts of PDN are more than pain alone. Early chapters of this thesis have outlined the existing evidence for PMPs for persistent pain (Chapter 1), and the current scarcity of evidence that exists for using these strategies with people who have PDN (Chapter 2). This chapter will describe an Internet survey study that asked people with PDN, of all the impacts of PDN they experienced, what did they most want help to manage better? The results will help to explore whether the priorities people report can be matched to strategies from PMPs.*

## *6.1 Introduction*

The qualitative interview study with patient participants presented in Chapter 4 demonstrated a range of opinions on the acceptability of physical activity and psychological coping strategies for managing PDN. Participants, who were keen to be active, wanted professional advice on activity to avoid flare of their pain. Other participants were sceptical that physical activity could have any beneficial effect on their pain experience. Participants with experience of psychological interventions felt these interventions were beneficial. Other participants were ambivalent to the role that psychological interventions could have on their pain.

The study in Chapter 4 also demonstrated that PDN impacted on many areas of life, far more broadly than represented by the outcome measures often used in quantitative epidemiological PDN research. For instance, the interview participants described a range of emotions including embarrassment and anger. They described the impact PDN had on their appetite and the subsequent effect this had on their diabetes management. They described significant social isolation, loss of independence and a reduction in their confidence to engage with society and the world around them. Impacts of this type are not frequently captured by existing outcome measures therefore incidence of the broad range of PDN impacts is unknown.

Only one study was located which asked people with PDN to identify their priorities for treatment (Schneider *et al.*, 2014). Increased activity levels (29.3%, CI 27.5 to 31%) and walking ability (24.4%, CI 22.8 to 26.1%) were identified by the participants as the most important outcomes (Schneider *et al.*, 2014). Whilst these results come from a large sample population (n=2245) participants were asked for their opinions on a restricted range of possible treatment priorities derived from the BPI (general activity, mood, walking, work, personal relations, sleep and life enjoyment). This restricted range may not have included the priorities that were most important to participants.

Analgesic treatment aimed at pain reduction can be considered successful from the population average change (Raskin *et al.*, 2014; Happich *et al.*, 2014; Hoffman *et al.*, 2010), but there are subgroups who appear to be 'non-responders' to medication (Moore, Derry and Eccleston, 2013). A large-scale meta-analysis of randomised controlled trials for neuropathic pain medication found NNTs of: 6.4 Duloxetine, 7.7 Pregabalin and 7.2 Gabapentin. The NNT statistic indicates how many patients need to be given the drug for one to get 30-50% pain reduction (Finnerup *et al.*, 2015). The NNTs suggest that significant proportions of people prescribed these medications experience little benefit in terms of pain reduction. These quantitative results were reflected by the participants' experiences of medication management outlined in Chapter 4; medication use was a balance between positive and negative affects but was rarely perfect in pain reduction and sometimes failed (Moore *et al.* 2013).

For other persistent pain conditions clinicians have developed multi-modal interventions using physical activity and psychological interventions to help people improve their overall quality of life with pain.

The recent Cochrane meta-review found that in many pathologies associated with persistent pain, physical activity had inconsistent effects on pain severity (Geneen *et al.*, 2017). Chapter 2 found few studies specifically investigating physical activity in PDN, and concluded that there was inconclusive evidence activity reduced pain. Both Geneen *et al.* (2017) and Chapter 2 suggested physical activity improves physical function, mental health and overall health-related quality of life. There was however notable scepticism amongst interview participants that physical activity was an appropriate form of treatment for PDN (Chapter 4).

Considering moods and thoughts, PDN has a close association with depression and anxiety. A longitudinal study of people with PDN found HADS scores worsened across an 18-month follow-up period (Vileikyte *et al.*, 2009). Multiple regression models demonstrated that baseline disability and unsteadiness on feet, but not pain intensity, were predictive of changes in depression at 18 months.

Research highlighted the relationship between depression and pain is bi-directional, with one worsening the other. Depression also has associations with altered behavioural responses, such as dietary choice and reduced activity engagement, these behavioural reactions to depression have subsequent impact on overall diabetes management (Jain *et al.*, 2011; Kiecolt-Glaser, 2010).

Two recent cross-sectional studies have examined the relationships between pain, cognitions, social state and function in people with PDN (Selvarajah *et al.*, 2014; Geelen *et al.*, 2016). Selvarajah *et al.* (2014) examined the contribution made to emotional distress by clinical,

social and cognitive factors. They found pain intensity contributed weakly to regression models for depression and did not contribute to models for anxiety. Social factors such as marital status were found to contribute to anxiety; and thoughts of helplessness (Pain Catastrophizing Scale sub-scale) contributed to both anxiety and depression to a greater extent than pain intensity. Geelen *et al.* (2016) conducted a study which examined the relationships between catastrophizing thoughts and pain-related disability (Geelen *et al.*, 2016). Multiple linear regressions identified significant association between pain catastrophizing and patient self-rating of reduced activity due to pain (Physical Activity Decline measure). Of importance, they found pain intensity did not significantly contribute to this association. The authors concluded that addressing patients' beliefs regarding pain and activity may have clinical utility. These studies demonstrate that associations exist between emotions, cognitions and function, in the population with PDN, as commonly found in other populations with persistent pain. These studies highlight that pain intensity has a small or non-existent role in mediating or predicting depression and anxiety. Recognition that thoughts, moods and function are interconnected, and subsequent challenge to these variables may help people with PDN to maintain function and quality of life.

There is a rationale for considering non-pharmacological management strategies in managing the impacts of PDN. However, there are two issues that must be considered, firstly the systematic review conducted as part of this thesis found a paucity of robust evidence to support strategies from PMPs being used with people who have PDN (Chapter 2). Secondly, and perhaps more importantly, the patient interview study highlighted that participants had mixed views on the appropriateness of such strategies, particularly the potential role of psychological help (Chapter 4). The majority of interview study participants had not experienced either psychological support or multi-disciplinary pain programmes, so their perspectives on these programmes were speculative. Those participants who had direct experience of PMPs felt there to be benefit to the strategies (see Chapter 4, section 4.10).

To move beyond pharmacological therapies and explore adjunctive management interventions that maybe applicable to the range of impacts experienced by people with PDN, the focus must be on patient experience and their priorities. This focus would ensure any interventions appear plausible and relevant to their issues, and hopefully increase engagement with these strategies. The interview study presented in Chapter 4 resulted in 68 individual codes that related to impacts of PDN. Due to the qualitative nature of the study and predominantly White British sample it cannot be assumed that the findings relate to the wider population with PDN.

The one previous study exploring patient treatment priorities (Schneider *et al.* 2014) had a large sample group, but was methodologically limited due to the narrow range of choices

presented to participants. The current study aimed to build on the range of impacts identified through patient interviews (Chapter 4) and use these to explore patient management priorities. The results will allow an exploration of whether patients' priorities can be mapped to existing management interventions.

*6.2 Study aims*

This study aimed to further understanding of the way PDN impacts on peoples' lives. It also aimed to develop understanding of the healthcare priorities patients have in helping them to manage these impacts.

The research objectives were:

1. To conduct an Internet survey exploring how people with PDN experience a range of PDN impacts, and the resulting effect on quality of life.
2. If sample size was sufficient, to explore whether respondents experience different impacts of PDN, dependent on a range of socio-demographic and clinical variables (measures of diabetes control and pain ratings).
3. To analyse whether there are associations with respondent pain coping strategies.
4. To list the top priority impacts of PDN which respondents most frequently want help to manage more effectively.
5. To analyse whether these priorities differ between sub-groups of respondents: by sex, type of diabetes, pain category and whether they have sought clinical help for their PDN or not.

The primary research questions were:

1. What were the impacts of PDN on quality of life as selected from an impact list informed by patient interviews?
2. What were the top priorities respondents have for support from healthcare services?

The secondary research questions were:

1. What were the frequencies respondents experience each of 58 statements on the impact of PDN?
2. For each statement endorsed, how did respondents rate the severity of impact on quality of life?
3. Were there associations between the impacts experienced and active/passive pain coping strategies?
4. Did the treatment priorities differ between subgroups of respondents?

*6.3 Methodology*

Surveys can be undertaken in a range of different ways including face-to-face, postal and via the Internet. For this study, the Internet was the preferred medium as it allowed wide ranging and quick marketing to potential respondents, responses can be anonymised easily and it is usually low cost.

A review of epidemiological studies showed only 2% of 2094 epidemiological articles published in high impact factor journals (2008-9) used Internet survey methods (Van Gelder, Bretveld and Roeleveld, 2010). Van Gelder *et al.* (2010) highlighted some challenges with electronic surveys: 1) Internet access is not universal, so this leads to an element of demographic selection bias and, 2) the data acquired from Internet surveys differed in reliability and validity to that acquired from face-to-face surveys. Other authors contend that these concerns have not been shown to effect the response rate or quality of data acquired through Internet surveys (Nicolaas *et al.*, 2014).

*6.4 Method*

UWE has a license with Qualtrics, an Internet survey service provider. Qualtrics provide an on-line service that aids with survey design, distribution and collection of results data.

*6.5 Ethical approval*

The UWE Health and Applied Sciences Faculty research ethics committee granted permission for this survey (HAS/15/11/038). As part of the survey design process an amendment was applied for due to changes in wording and structure of the survey. The amendment was granted approval (12/1/16, Appendix 20).

*6.6 Diagnostic screening questions*

This survey required the development of a short series of screening questions to allow identification of people with PDN by self-report. PDN has some variation in presentation and possible delay in diagnosis (Daousi *et al.*, 2004; Sadosky, Hopper and Parsons, 2014); thus, if *Diagnosis of PDN by a medical professional* had been set as a strict inclusion criterion, many people who have the condition might have been excluded. A set of screening questions were developed in conjunction with Professor David Wynick (Consultant Endocrinologist, and national PDN specialist, University Hospitals Bristol NHS Foundation Trust) that were intended to rigorously screen for the clinical features of PDN.

1. Do you often have pain or odd sensations in your feet? Y/N
    a. If Y - one or both?
2. Do you often have pain or odd sensations in your hands? Y/N

   a. If Y - one or both?
3. At what time of day is the pain in your feet (and hands) worse? Night, day, no pattern.
4. Have you had a diagnosis from a health care professional that the pain in your feet (and hands) is related to, or a complication of, your diabetes? Y/N

The majority of people with PDN would be expected to report pain, in both feet (hand symptoms tend to develop over time), which is worse at night (Tesfaye *et al.*, 2010).

*6.6.1 Inclusion criteria*

- Self-reported diagnosis of type 1 or type 2 diabetes.
- Self-reported clinical diagnosis of PDN, or:
- Self-reported symptoms indicative of a diagnosis of PDN (bilateral foot pain, possible additional bilateral hand pain, worse at night), even without a clinical diagnosis.

*6.6.2 Exclusion criteria*

- Self-reported symptoms, which were inconsistent with a likely diagnosis of PDN (unilateral foot pain, hand pain without foot pain).
- No Internet access.

Internet surveys cannot provide certainty that the inclusion criteria are met because they rely on self-report rather than objective clinical criteria, however this screening process was felt likely to rule out respondents who did not have PDN.

*6.7 Survey design process*

The research student initially created the survey online, using Qualtrics. Substantial sections of the survey asked patients to reflect on the influence PDN had on their quality of life. Whilst the definition of "quality of life" is varied and contested (Barcaccia *et al.*, 2013), this study used an amended WHO definition. The WHO consider quality of life to be wholly subjective and comprising of both positive and negative aspects of a person's "physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment" (WHO, 1995). The final part of the definition was felt to lack clarity for the average reader which may have resulted in a high drop-out rate. The wording of the survey questions asked respondents to consider whether each impact had any effect on "their physical health, psychological state, level of independence, social relationships *and their freedom to move around their environment as you would expect*".

Respondents were asked to consider each impact statement and score its influence on their quality of life, using a 5-point Likert scale. The scale was described as: 0=do not experience this

impact, 1=experienced but no impact on QoL, 2=experienced and minimal impact on QoL, 3=experienced and moderate impact on QoL and 4=experienced and large impact on QoL.

The impact statements were developed directly from the interview study with patients (Chapter 4, section 4.5). Each NVivo code identifying an impact of PDN (n=68) was considered for inclusion. A statement was written reflecting the nature of the impact on the person with PDN. Eleven codes were excluded because they were either near duplicates, the code reflected a positive counterpoint to the usual difficulties of PDN, the participants were transitory, or they were statements of impact made by a partner (please see Table 12).

Table 12 - Impact codes excluded from survey

| **Impact code excluded** | **Reason for exclusion** |
|---|---|
| *Sleep not disturbed* | Positive counter point |
| *Able to work* | Positive counter point |
| *Carry on with social life* | Positive counter point |
| *Changing jobs* | Transitory impact |
| *Returning to work* | Transitory impact |
| *Advice for foot care* | Not a direct impact of PDN |
| *Foot position* | Pain management strategies could not alter this |
| *Always been independent* | Combined with *Loss of independence* |
| *Chronic pain* | Related to chronic pain other than PDN |
| *Knowing I can't help* | Impact on partner of interviewee |
| *Templar torture* | Combined with other impacts related to subjective pain experience |

Prior to undertaking a pilot phase the survey was trialled with two EPRPs. The role of EPRPs has been discussed previously (see Chapter 3, section 3.12). Both EPRPs had been participants in the patient interview study and had contributed directly to the development of the survey impact statements. They had given consent to be contacted about future studies. The EPRPs met individually with the research student and Professor Fiona Cramp, who took written notes. No audio or video recordings of these meetings were made, and any data obtained by completing the survey were deleted.

The aims of the meetings were to ensure the structure of the survey appeared logical, that the language used in the questions was clear and not ambiguous (face validity), and finally that EPRPs read and understood the impact statements with the same intention as the research student (content validity). As the EPRPs read through the PIS and completed the survey online,

they were asked to verbalise their thoughts, to explain what they thought the questions were asking and what they thought the impact statements referred to. The resulting discussion was then used to refine the survey, prior to a pilot phase.

The changes to wording of the impact statements following the meetings with the EPRPs have been summarized in Table 13.

Table 13 - Development of survey wording

| Issues raised by EPRP | Original phrase/question | Revised phrase/questions |
|---|---|---|
| **Symptoms experienced are not always best described as pain** | Do you often have pain in your feet/hands? | Do you often have pain or odd sensations in your feet/hands? |
| **People have routine medication and pain flare-up medication** | Please select medications used for PDN | 1 - Please select medications used routinely for PDN<br>2 - Please select medications used for pain flare-ups of PDN |
| **Term 'mean' was felt too harsh** | When PDN flares up I can be mean to those around me | When PDN flares I can be less tolerant to those around me |
| **Keeping PDN to one's self depended on social context** | I keep my problems with PDN to myself | 1 – I keep my problems with PDN from those around me<br>2 – I keep my problems with PDN from my wider social network |
| **Wanted to clarify a choice was made to restrict or stop driving** | PDN affects my ability to drive | PDN makes me think about driving carefully |
| **EPRP had an emotional response to the breadth of impacts portrayed** | | Added further signposting to support for PDN at the end of the survey |

EPRPs considered that presenting 58 statements, from which to choose three, was impractical. A tension existed between either, presenting all 58 statements and leaving respondents free to choose their top priorities, or grouping the statements and therefore making the prioritisation process more manageable. One grouping option was to ask respondents to choose priorities from the statements they rated most impactful on their quality of life, for instance ≥3/4 on the Likert scale. This was discounted because it would stop respondents from prioritising impacts that were less severe, but experienced more frequently, than the more severe but less frequently experienced impacts.

Another option was to group the impacts by the type of impact, (see column in Appendix 19). The researcher had externally imposed these categories (mood, function, social, sensory, rest

etc.) onto the coded interview data and they had not been endorsed by people with PDN. Respondents needed freedom to choose those statements that were most important to them. Being forced to choose, for instance, one impact statement from each category would 1) impose the structure that all categories were equally relevant and 2) impose categorisation from the perspective of the researcher, a clear source of researcher bias.

It was clear from the meeting with EPRPs that asking participants to prioritise three items out of 58 could result in a large number either not completing the process, or not giving a fully considered response. A two-stage process was subsequently designed to break down the task. Firstly, the respondents would select a short-list of up to ten impacts that were most important to them. They would subsequently rank these choices with 1=top priority for management, through to 10=tenth priority for management. This process allowed respondents to self-limit the number of impacts that were most important to them.

*6.7.1 Survey pilot phase*

A pilot phase was undertaken to test the process of the online survey. An information pack was created which contained a covering letter, PIS for the pilot survey and a further sealed envelope that contained the PIS for the full survey. The pilot PIS letter asked people to open the full survey envelope if they were willing to take part. The process was initially tested on two research colleagues who were naïve to the research study. They were specifically asked to highlight any unclear text or instructions. Some language was amended as a result of their feedback. Participants from the interview study who had given permission to be contacted about future research were subsequently sent the pilot information pack, see Appendix 19.

The pilot survey included two extra questions. Firstly, responders were asked to input their study number, which was contained in the pilot information. This number allowed the researcher to identify who had completed the pilot survey, and only send reminder letters to non-responders. A reminder was sent two weeks after the initial request, after which there was no further attempt to recruit to the pilot. A final free text question provided the respondents with an opportunity to make comments about the survey. These could be technical issues they experienced, language or wording issues or any other comments that they believed to be relevant.

*6.7.2 Results of the pilot survey phase*

There were eight responses to the pilot survey, a 34% opt-in rate, with all respondents completing the survey in total (0% drop out rate). The duration of time to compete the survey ranged from 22 to 43 minutes (mean 32 minutes). Based on these responses, the PIS was updated to reflect the likely time required to complete the survey.

In the free text responses, there were two themes: firstly, related to the choice of impacts to prioritise. One respondent had difficulty dragging the choices to the short list box, another commented on the range of options (58 statements). The second theme contained comments that respondents wanted more information on PDN, particularly the causes. Signposts to sources of further information on PDN were added at the end of the survey.

Three respondents contacted the research student by email or phone because they were unable to access the survey on-line. The pilot PIS contained a website address URL that the respondents were required to put into their Internet browser manually (https://tinyurl.com/npv9kz7). There were some difficulties with this process. The final survey was delivered by email and on websites, so the web address for the survey was an automated hyperlink. This was felt to overcome the problems the pilot respondents had faced.

The comments from the pilot respondents can be found in Appendix 21. The final survey structure is outlined in the following section.

## *6.8 Final survey content*

### *6.8.1 Screening questions [4 questions]*

The four diagnostic screening questions described in section 6.6.

### *6.8.2 Demographic Information [10 questions]*

This included: sex, age, ethnicity, type of diabetes, duration of diabetes and PDN symptoms, current analgesia for PDN (routine and during a flare-up), home status (living alone, with partner, with family or other) and work status (working, retired, unemployed or other). Respondents were asked to rate their average pain for the past week (0-10 NRS).

### *6.8.3 Self-rating of diabetes control [1 question]*

This question was important because sub-optimal glycaemic control tends to be associated with development and severity of PDN. The wording of the question was developed with Professor Wynick.

"From my own blood monitoring and discussions with health professionals I consider the management of my blood sugars as: very good, good, moderate, poor or very poor."

### *6.8.4 Coping Strategies Questionnaire (CSQ) [14 questions]*

This investigated the use of different coping styles for chronic pain and has been validated for neuropathic pain (post herpetic neuralgia (Haythornthwaite *et al.*, 2003)). The CSQ characterises respondents as using either active or passive coping strategies. Active coping styles

are associated with improved functioning and adjustment with living with persistent pain compared with passive styles (Jensen *et al.*, 2003; Snow-Turek, Norris and Tan, 1996). It is important to characterise respondents in this way because recent studies have shown catastrophizing thoughts (passive coping) contributed to both anxiety and depression (Selvarajah *et al.*, 2014) and reduced physical activity (Geelen *et al.*, 2016).

*6.8.5 Impact of PDN [58 statements]*

*Part 1 – frequency and severity of impact on quality of life.*

Respondents were asked to read a list of 58 impact statements. The development of these statements has been described in section 6.7, the full list can be found in Appendix 18. They were invited to rate on a 5-point uni-polar Likert scale, whether they experienced each impact and if so how their experience of this impact affected their quality of life. These impacts were randomised in the order they were presented to each respondent.

There was a free text section for respondents to add other impacts they did not feel were represented in the presented list. This free text response allowed for the possibility that the interview study (see Chapter 4) did not gather data fully representative of the UK PDN population.

*Part 2 – priorities for help with management*

Respondents were asked to consider the 58 impact statements, then short list up to 10 of the impacts, and place in order of priority for which they wanted better management.

Finally, two questions asked if they had sought clinical help for their experience of PDN (y=help-seeking population, n=not help-seeking population) and if so, from whom (diabetes consultant, pain consultant, practice nurse, diabetes specialist nurse, GP, podiatrist, physiotherapist, psychologist, other (free text) – multiple selection possible).

*6.9 Sampling and recruitment strategy*

In order to obtain results with the greatest possible validity and relevance to the broader PDN population, this study sought responses from a wide range of people with PDN. PDN becomes more common as people age (Shakher and Stevens, 2011), so sampling hoped to include older adults (60yrs+). PDN affects people with T1 and T2DM and both sexes. Diabetes has higher prevalence rates in South Asian and other minority ethnic groups (Gujral *et al.*, 2013). The interview study from which the impact statements were derived was not ethnically diverse, so it was important to access people from different ethnic backgrounds.

DUK support was secured to market this research study. Diabetes peer-support group networks run nationwide and are organised by local people. Peer-support group meetings are

held in venues and locations that are accessible to the local population with diabetes. DUK actively work to encourage engagement in self-managing diabetes in areas of social deprivation and from ethnic minorities (DUK, 2015), as these populations are more at risk of diabetes and the associated complications (Claydon, Campbell-Richards and Hill, 2013). This study used the communication processes that exist between DUK, the peer support group organisers and their members to market this survey. The membership profile of DUK was outlined in section 3.5.2.3.

The study was also posted on Internet discussion forums that focussed on PDN. Patient forums hosted by DUK (diabetes.org.uk), Diabetes Forum (diabetes.co.uk) and Diabetes-support (diabetes-support.co.uk) were used. New threads were started to maintain the study information near the top of forum listings and the wording of the headline was altered to encourage participation. These processes for recruitment were active between February and April 2016

Each of these strategies for recruitment included a webpage address to access the survey. Office for National Statistics data suggested that 76% (CI 74-78%) of UK adults access the Internet on a daily basis. On average people aged over 65 years access the Internet at least daily (42%) or weekly (13%); they use a significant amount of this access for researching goods and services (44%) (ONS, 2014). These data suggested the survey recruitment strategies had a good chance of reaching the desired populations.

*6.10 Data analysis*

The sample sociodemographic and clinical data were analysed with descriptive statistics. Descriptive and frequency data analysis were conducted to describe the number and percentage of respondents who did not experience (0 on the Likert scale), or did experience (1-4 on the Likert scale) each impact statement.

The free text responses identifying additional participant impacts not included within the list of statements, were collated. The researcher compared these free text comments against the existing code structure developed in the patient interviews, to identify whether there were new impacts the interviews had not described (Braun and Clarke, 2006). A second independent research supervisor verified this process and the findings were discussed with the supervisory team.

Principal Component Analysis (PCA) was used to reduce the 58 impact statements to a smaller number of summary indices. These summary indices were explored for any correlations with sociodemographic (home status, work status, age and sex) and clinical subgroups (diabetes well/not well controlled, and pain ratings).

The CSQ data were compared against data from the same measure used with other neuropathic pain conditions. Cohen's *d* (Cohen, 1988) was used to investigate any statistical difference in coping strategies between these two data samples. Correlation analyses were performed between the pain CSQ and the impacts identified by respondents. In the event of missing data, if respondents had rated more than 51 questions (85%) from the survey section, the mean impact rating was used for imputation for the missing data point(s). If respondents rated fewer than 85% of the impacts, then their case was excluded from the analysis. Histograms were used to check for normal distribution and Pearson's correlation statistic used to examine correlations between impact and coping style.

The analysis of respondent priorities was based on similar research investigating the priorities patients had for pharmacological management of rheumatoid arthritis (Sanderson *et al.*, 2010). The priorities assigned to impacts by respondents were transformed using an inverse scale (1st priority=10, 2nd priority=9 … 10th priority=1, not selected=0). For each impact these scores were summed. This sum was presented as a percentage of the possible maximum priority.

For example – if 10 respondents had endorsed an impact as one of their priorities, and all respondents were to rate it their highest priority (reverse score 10), the maximum sum would be 100/100 or 100%. If their reversed scores actually sum 40, this impact would be calculated at 40/100 or 40%. Presenting the data in this way, rather than a simple sum of priorities has two benefits for the analysis. Firstly, it helped to address the balance between many respondents rating an impact as a low priority choice, and few respondents rating an impact as a high priority. Were scores to have been summed, an impact rated first priority by two respondents (2x10=20) would have the same weighting applied as an impact rated fifth priority by four respondents (4x5=20). This approach used the ratio percentage to account for the number of respondents who endorse an impact as a priority. Using the examples above, two respondents rating an impact first priority 20/20 or 100%, or four respondents rating an impact fifth priority 20/40 or 50%.

Secondly, this approach ensured the calculation of impact priority was done for each impact, not each respondent. Respondents who selected more priority impacts would not have undue influence on the data, compared to respondents who may have selected fewer than 10 impacts as priorities.

Descriptive analysis explored whether different priorities existed by respondent's sex, type of diabetes, pain levels and whether they had sought help for the impacts of PDN they experienced.

All analyses were performed using either Microsoft Excel 2011 for Mac (Microsoft Corporation, California 2010) or IBM SPSS v22 (IBM Corporation, 2015) as appropriate.

*6.11 Results*

There were 107 individual responses to the survey with 78 eligible data sets once the case definition was applied. Overall there was a dropout rate of 40%; this occurred either early in the survey at the demographic and clinical sections or, for those who described meeting the eligibility criteria, later in the survey when asked to rate the 58 impact statements. A sample of 62 completed the survey in full.

*6.11.1 Sample demographics*

The sample (n=78, see Table 14 below) of eligible respondents included 43 women (55%) female, and had a mean age of 57 (SD13) years. Forty-nine respondents (63%) had T2DM and 26 (33%) had T1DM. Sixty-eight respondents (87%) self-rated their glycaemic control as very good, good or moderate, with nine (13%) rating their control as poor or very poor and one missing data item. Respondents had been diagnosed with diabetes for a mean 17.8 (SD13.7) years and had symptoms of PDN for a mean 7.3 (SD6.3) years. Respondents were retired (n=36, 46%), employed (n=26, 33%) or unemployed (n=11, 14%). Seventy respondents (90%) of the sample identified as White British.

Table 14 - Internet survey respondent characteristics

| ***Characteristic*** | N=78 | % or Mean ± SD (range) |
|---|---|---|
| ***Sex*** | | |
| ***Male*** | 35 | 45% |
| ***Female*** | 43 | 55% |
| ***Ethnicity*** | | |
| ***White British*** | 70 | 90% |
| ***Asian/Asian British*** | 3 | 4% |
| ***Mixed ethnic groups*** | 1 | 1% |
| ***Other (White non-British, White Irish, Hispanic and European)*** | 4 | 5% |
| ***Work status*** | | |
| ***Employed*** | 26 | 33% |
| ***Unemployed*** | 11 | 14% |
| ***Retired*** | 36 | 46% |
| ***Other*** | 4 | 5% |
| ***Missing*** | 1 | 1% |
| ***Home status*** | | |
| ***Living alone*** | 22 | 28% |
| ***Living with partner*** | 34 | 43% |
| ***Living with family members*** | 21 | 27% |
| ***Other*** | 1 | 1% |
| ***Type of diabetes*** | | |
| ***Type 1*** | 26 | 33% |
| ***Type 2*** | 49 | 63% |
| ***Missing*** | 3 | 4% |

| ***Characteristic*** | N=78 | % or Mean ± SD (range) |
|---|---|---|
| ***Self-rating of diabetes management*** | | |
| ***Very good*** | 18 | 23% |
| ***Good*** | 22 | 28% |
| ***Moderate*** | 28 | 36% |
| ***Poor*** | 4 | 5% |
| ***Very poor*** | 5 | 6% |
| ***Missing*** | 1 | 1% |
| ***Age*** | | 57 ± 13 (26-84 years) |
| ***Diabetes duration*** | | 17.8 ± 13.7 (1-57 years) |
| ***PDN duration*** | | 7.3 ± 6.3 (1-33 years) |
| ***Average pain score past week (0-10)*** | | 6 ± 2.4 |

Table 15 outlines the analgesic medication used by the respondents (n=78). Twenty (26%) did not use any regular medication for managing PDN, 41 (53%) were using medications as recommended by NICE for the management of PDN (NICE, 2013a). Individuals were most commonly using one class of medication (mode=1) but the range extended from nil to five classes of medication. Respondents were using multiple medications so responses total more than 100%.

When PDN flared, the sample respondents increased the use of weak opioids such as Tramadol and Co-codamol.

Table 15 - Internet sample medication use

| *Medication class* | Regular use n=, (%) | Flare up use n=, (%) |
|---|---|---|
| ***Anti-epileptics (Pregabalin or Gabapentin)*** | 23 (29%) | 15 (19%) |
| ***Amitriptyline*** | 10 (12%) | 7 (9%) |
| ***Duloxetine*** | 8 (10%) | 3 (4%) |
| *Sum total of NICE recommendation medication* | **41 (53%)** | **25 (32%)** |
| ***Over the counter analgesia (Paracetamol or ibuprofen)*** | 23 (29%) | 23 (29%) |
| ***Weak opiates (Co-codamol or Tramadol)*** | 11 (14%) | 28 (35%) |
| ***Strong opiates (Morphine)*** | 9 (11%) | 8 (10%) |
| ***Pain patch*** | 4 (5%) | 1 (1%) |
| ***Capsaicin cream*** | 3 (4%) | 2 (2%) |
| ***Other medications*** | 13 (16%) | 13 (16%) |
| *Nil medication* | **20 (26%)** | **15 (19%)** |

### *6.11.2 Impact based on frequency*

Table 16 shows the ten most frequently experienced impacts.

Table 16 - Ten most experienced impacts of PDN

| ***Impact statement*** | ***% Experienced (1-4 Likert), n=62*** |
|---|---|

| | |
|---|---|
| *I have to check my feet regularly for possible injury* | **94.8** |
| *I am worried that my PDN will get worse in the future* | **93.4** |
| *My sleep is disturbed due to PDN* | **91.8** |
| *PDN causes me to have numb feet* | **91.7** |
| *PDN leads me to get frustrated* | **89.7** |
| *My feet look normal but I have this severe pain* | **88.7** |
| *PDN affects my ability to concentrate* | **86.7** |
| *PDN gives me a sense of restless legs* | **85.0** |
| *When PDN flares up I can be less tolerant to those around me* | **84.5** |
| *PDN makes walking difficult* | **83.6** |

Table 17 shows the ten least frequently experienced impacts. Only the last four impacts – frequent cramps, headaches, memory difficulty and suicidal ideation were endorsed as experienced by less than half the respondent sample. The complete list of all impact statements can be found in Appendix 22.

Table 17 - Ten least experienced impacts of PDN

| ***Impact statement*** | ***% Not experienced (0 Likert), n=62*** |
|---|---|
| *PDN makes me worried about going out of the house* | **44.1** |
| *PDN makes me feel embarrassed* | **44.6** |
| *My PDN affects my close family* | **44.8** |
| *It bothers me what other people think of me due to the problems I have with PDN* | **45.0** |
| *I worry how our money will be affected because of PDN* | **45.8** |
| *I get more breathless than before I had PDN* | **48.2** |
| *I get cramp more frequently than before I has PDN* | **50.0** |
| *PDN affects my memory* | **50.8** |
| *PDN can lead me to have headaches* | **53.4** |
| *I have contemplated suicide due to my PDN* | **70.7** |

### *6.11.3 Impact based on severity*

Table 17 and 18 show the impacts as rated by severity of impact on quality of life. Table 18 shows the ten most severe impacts; these were the summed responses 3 and 4 on the Likert scale ('moderate' and 'large' impact). These most severe impacts included: worry for the future (84%), perceptions of others (76%), cramp (76%), sleep disturbance (75%) and frustration (75%).

Table 18 - Ten most severe impacts of PDN

| ***Impact statement*** | ***% 3/4 or 4/4, n=62*** |
|---|---|
| *I am worried that my PDN will get worse in the future* | **84.2** |
| *It bothers me that other people can't see I have this problem* | **76.3** |
| *I get cramp more frequently than before I has PDN* | **75.9** |
| *My sleep is disturbed due to PDN* | **75.0** |
| *PDN leads me to get frustrated* | **75.0** |
| *PDN affects a wide range of activities that I want to do* | **75.0** |
| *PDN causes me to have numb feet* | **74.5** |
| *PDN can lead me to have headaches* | **74.5** |
| *I have reduced my physical activity due to PDN* | **74.5** |
| *PDN affects my social life* | **74.2** |

Table 19 shows the ten least severe impacts; these were the summed responses 1 and 2 on the Likert scale ('no' and 'small' impact).

Table 19 - Ten least severe impacts of PDN

| ***Impact statement*** | ***% 1/4 or 2/4, n=62*** |
|---|---|
| *PDN hurts so much it brings tears to my eyes* | **41.7** |
| *My skin is sensitive to the lightest touch* | **43.1** |
| *PDN makes me feel embarrassed* | **44.4** |
| *PDN affects my appetite for food* | **44.8** |
| *I get more breathless than before I had PDN* | **44.8** |
| *I worry how our money will be affected because of PDN* | **45.5** |
| *I don't understand why I have PDN* | **47.1** |
| *My overall quality of life is really affected by PDN* | **51.4** |
| *PDN affects our family holidays* | **51.9** |
| *PDN and balance problems lead me to fall over* | **52.9** |

The decrease in impact severity from top rated (84.2%) to bottom rated (52.9%) across 58 impact statements has been plotted as a graph (Figure 19). The full list of impacts based on severity of effect on quality of life can be found in Appendix 23.

*6.11.4 Analysis of free text additions*

Fifteen respondents added free text. The full transcripts of this text can be found in Appendix 24. This text was assessed against the code structure from the patient interviews and 30 codes were identified. Twenty-seven codes were already in existence but three new codes were required to accommodate issues that had not been raised previously: autonomic neuropathy; self-harming behaviour and hand numbness.

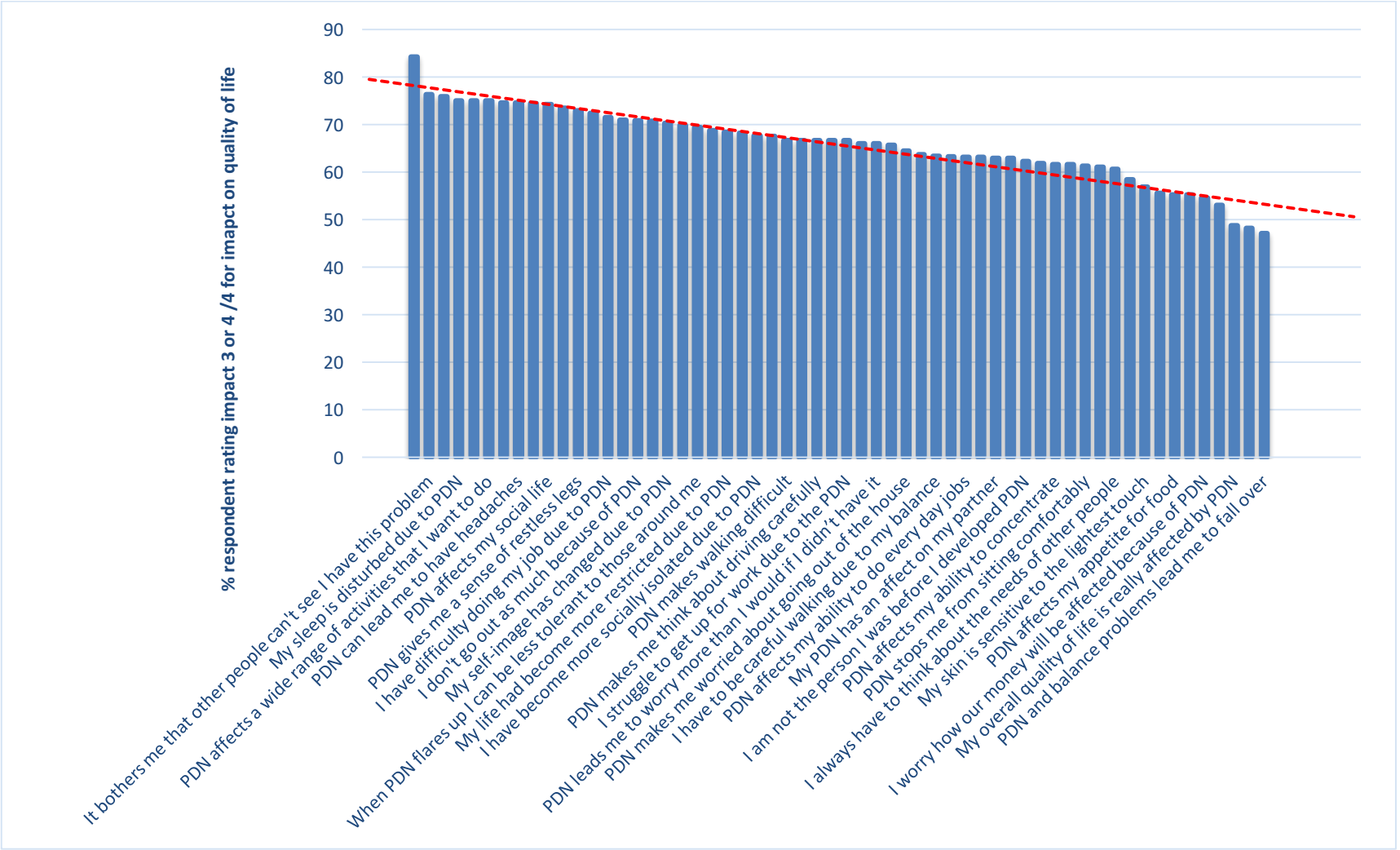
*6.11.5 Principal Component Analysis*

The study protocol included PCA to reduce the 58 impact statements to a smaller number of summary indices (Floyd and Widaman, 1995). Calculations of precise sample sizes required for PCA are contentious. A precedent in literature suggests 5-10 participants per variable with a minimal sample size of at least 100-200 participants. A counter argument examines the factor loading size within a calculated solution, as a measure of stability of that solution (Floyd and Widaman, 1995). A sample size of 500 was set as sufficient, with at least 20 responses per variable to be analysed. This sample was not achieved meaning that PCA could not be supported.

*6.11.6 Correlation between impacts of PDN and the Coping Strategies Questionnaire (CSQ)*

Visual inspection of the data set showed some missing data. After discussion with the supervisory team, the following strategy was adopted in order to maximise the dataset. If respondents had completed more than 51 questions (85%) of this section, the mean impact score for that case was calculated and this value used to replace missing data points. This approach aimed to maximise the useable dataset, by retaining cases that would otherwise be discarded due to a few missing items in the survey. The approach of *overall* mean imputation (using the whole sample mean to replace a missing data point) has precedent in literature (Donders *et al.*, 2006) but is known to reduce the extent of sample deviation. Replacement with individual case mean imputation was felt appropriate to minimise the statistical shift that was inevitable. This process was applied to five cases that had omitted fewer than 7 (15%) of the questions, providing a sample of n=48 for analysis.

Figure 19 - Impacts with most effect on quality of life



The CSQ was scored for each subscale in line with Jensen *et al.* (2003). The overall score for Active coping was the sum of Diverting attention, Reinterpreting pain sensations, Coping with pain and Activity. The Passive coping score was the sum of Catastrophizing and Praying/Hoping; these are in line with literature recommendations (Snow-Turek *et al.* 1996).

The descriptive results for the CSQ can be seen in Table 20, higher scores represent greater use of that coping strategy. Table 20 presents comparison data from a survey of 68 people with PHN, a neuropathic pain condition subsequent to Herpes Zosta virus (Haythornthwaite *et al.*, 2003). The mean and standard deviation data from these studies have been used to calculate the effect size between these sample populations (Cohen, 1988).

Table 20 - Pain Coping Strategies Questionnaire (CSQ) descriptive results

| ***Coping domains*** | ***Mean (SD), n=48*** | ***Comparison data, mean (SD) [a], n=68*** | ***Cohen's effect size (d)*** |
|---|---|---|---|
| *Diverting attention (DA)* | 3.98 (3.40) | 2.27 (1.5) | 0.65 |
| *Reinterpret sensations (R)* | 3.76 (2.89) | 0.86 (1.2) | 1.31 |
| *Coping (Co)* | 5.69 (3.46) | 3.34 (1.5) | 0.88 |
| *Activity (Act)* | 5.94 (3.04) | 2.80 (1.2) | 1.35 |
| *Ignore sensations (Ig)* | 4.89 (3.60) | 2.19 (1.2) | 1.00 |
| ***Active coping (DA, R, Ig, Co and Act)*** | **24.03 (11.71)** | - | - |
| *Catastrophizing (Cat)* | 5.67 (3.86) | 1.72 (1.3) | 1.37 |
| *Praying/Hoping (Pr)* | 4.76 (3.44) | 3.44 (1.7) | 0.48 |
| ***Passive coping (Cat and Pr)*** | **10.36 (6.42)** | - | - |
| [a] *Haythornthwaite et al. 2003* | | | |

*6.11.6.1 Correlation of CSQ with total number of impacts experienced*

The total number of impacts experienced was any impact statement scored 1-4 on the survey. Missing data were not imputed for these variables. It was not appropriate to assume that a respondent had missed a specific question by oversight, rather than omitted it for other reasons.

A correlation was then calculated between the total number of impacts experienced and Active and Passive CSQ scales. For all the analyses, histograms were plotted and data were checked for normal distribution. A normal distribution was approximated for all supporting the calculation of Pearson's correlation statistic.

Table 21 outlines the correlation results. There was significant correlation between the number of impacts experienced and CSQ Passive coping scale ($r=0.537$, $p<0.001$). As the degree of passive coping increases, so do the number of experienced impacts. There was no significant correlation between CSQ Active coping and experienced impacts ($r=0.235$, $p=0.156$).

*6.11.6.2 Correlation of CSQ with the mean severity of impacts experienced*

Any missing impact severity data were replaced with the individual case mean as previously described (Section 6.10). This process ensured cases were complete for inclusion in the calculation, rather than adding any impact to the case profile.

There was significant correlation between the mean severity of impacts experienced and CSQ Passive coping scale (r=0.587, p<0.001). As passive coping strategies increased, so did the mean severity of impact on quality of life, for the impacts experienced. There was no correlation between CSQ Active coping and mean severity of impacts experienced (r=0.019, p=0.905), see Table 21.

*6.11.6.3 Correlation of CSQ with the total severity of impacts experienced*

The total severity score was calculated by calculating the sum of the impact ratings (Likert 1-4) for each impact endorsed by the respondents. This provided a metric that reflected both the count and severity of the impacts experienced.

There was significant correlation between the sum for total impacts experienced and CSQ Passive coping scale (r=0.619, p<0.001). As passive coping strategies increased, so did the total score of impacts experienced. There was no significant correlation between CSQ Active coping and total severity of impacts experienced (r=0.155, p=0.32), see Table 21.

Table 21 - Correlation results for CSQ and impacts of PDN

| | ***CSQ Active coping*** | ***CSQ Passive coping*** |
|---|---|---|
| ***Impact count (n=43)*** | r=0.235, p=0.156 | r=0.537**, p<0.001 |
| ***Mean impact severity (n=48)*** | r=0.019, p=0.905 | r=0.587**, p<0.001 |
| ***Total impact severity (n=48)*** | r=0.155, p=0.32 | r=0.619**, p<0.001 |
| ***. Correlation is significant at the 0.01 level (2-tailed).* | | |

*6.11.7 Seeking help for PDN*

Thirty-seven respondents (60.7%) had sought help from clinicians, see Table 22 below. Three professional groups were mainly represented – GPs (31.8%), podiatrists (20.6%), and Diabetes consultants (16.8%). These professions total 69.2% of the clinicians consulted. DSNs accounted for 3% of the clinicians consulted for help managing PDN.

Table 22 - Have you sought help for your PDN?

| *Have you sought help from any health professional to help you to cope with PDN?* | *n (%)* |
|---|---|
| Yes | 37 (60.7) |
| No | 24 (39.3) |
| *If yes, who from…* | |
| GP | 34 (31.8) |
| Podiatrist | 22 (20.6) |
| Diabetes consultant | 18 (16.8) |
| Physiotherapist | 9 (8.4) |
| Pain consultant | 8 (7.5) |
| Diabetes specialist nurse | 3 (2.8) |
| Psychologist | 3 (2.8) |
| Other - Cardiovascular consultant | 1 (1.9) |
| Other - Neurologist | 1 (1.9) |

### *6.11.8 Patient priorities for help in managing PDN*

Overall, 56 of 58 impacts were rated as a priority by at least one respondent. Tables 21-26 contain a percentage column that displays the sum of priority ranking, as a percentage of the potential maximum for the respondents in that sub-group (for example, if n=78, (x/780)*100, where x=the sum of priority score). The approach to analysis for this stage of the study can be found in Section 6.10 Data analysis.

From the sample as a whole (Table 23) the most reported top priorities were: sleep disturbance (21.9% of maximum possible priority); followed by worry about physical fitness (14.1%), numb feet (13.5%), difficulty walking (12.1%), worry that PDN will worsen in the future (11.5%) and depression associated with PDN (11%).

Table 23 - Top 10 priorities for management of PDN impact

| ***Impact statement*** | *Overall %, n=78* |
|---|---|
| *My sleep is disturbed due to PDN* | 21.9 |
| *I worry about keeping my physical fitness due to PDN* | 14.1 |
| *PDN causes me to have numb feet* | 13.5 |
| *PDN makes walking difficult* | 12.1 |
| *I am worried that my PDN will get worse in the future* | 11.5 |
| *PDN leads me to feel depressed* | 11.0 |
| *PDN gives me a sense of restless legs* | 10.0 |
| *PDN makes it difficult to buy shoes that are comfortable* | 10.0 |
| *I have to be careful walking due to my balance* | 10.0 |
| *PDN leads me to get frustrated* | 8.8 |

The least reported priorities were: affected appetite, changes to self-image, not coping with PDN (all <1%), and lastly, restricted dancing and thinking of others, both with 0% priority (Table 24).

Table 24 - 10 least priorities for management of PDN impact

| ***Impact statement*** | *Overall %, n=78* |
|---|---|
| *I have difficulty doing my job due to PDN* | 1.2 |
| *I struggle to get up for work due to the PDN* | 1.0 |
| *PDN can lead me to have headaches* | 1.0 |
| *My PDN affects my close family* | 1.0 |
| *It bothers me what other people think of me due to the problems I have with PDN* | 1.0 |
| *PDN affects my appetite for food* | 0.9 |
| *My self-image has changed due to PDN* | 0.8 |
| *I don't cope well with PDN* | 0.1 |
| *PDN has stopped me going dancing* | 0.0 |
| *I always have to think about the needs of other people* | 0.0 |

#### *6.11.8.1 Priority by sex*

When priorities were examined based on respondent sex, sleep remained the top priority for men (25.1%) and women (19.3%) (Table 25). Physical fitness remained in the top four for both sexes (Male 4$^{th}$ 14%, Female 2$^{nd}$ 14.2%). Walking related issues were a priority for both sexes but for different reasons with men identifying balance as an issue (12.9%) and women identify the purchase of comfy shoes as difficult (13.3%).

Table 25 - Priorities by sex

| ***Impact statement*** | *Male %, n=35* | *Female %, n=45* | ***Impact statement*** |
|---|---|---|---|
| *My sleep is disturbed due to PDN* | 25.1 | 19.3 | *My sleep is disturbed due to PDN* |
| *PDN causes me to have numb feet* | 17.1 | 14.2 | *I worry about keeping my physical fitness due to PDN* |
| *I have to be careful walking due to my balance* | 16.3 | 13.3 | *PDN makes it difficult to buy shoes that are comfortable* |
| *I worry about keeping my physical fitness due to PDN* | 14.0 | 13.0 | *I am worried that my PDN will get worse in the future* |
| *PDN makes walking difficult* | 12.9 | 11.4 | *PDN makes walking difficult* |
| *PDN affects my ability to do every day jobs* | 12.3 | 11.2 | *PDN gives me a sense of restless legs* |
| *PDN leads me to feel depressed* | 11.4 | 10.7 | *PDN leads me to feel depressed* |
| *When PDN flares up I can be less tolerant to those around me* | 10.3 | 10.7 | *PDN leads me to get frustrated* |
| *I have lost confidence to be myself due to PDN* | 10.3 | 10.5 | *PDN causes me to have numb feet* |
| *I am not the person I was before I developed PDN* | 10.0 | 9.8 | *I have to check my feet regularly for possible injury* |

*6.11.8.2 Priority by type of diabetes*

Sleep remained the top priority irrespective of the respondent's type of diabetes (Type 1 27.7%, Type 2 20.2%) (Table 26). The two subgroups similarly prioritised issues affecting their fitness and issues that maybe related to their walking (balance, cramp and numbness).

Table 26 - Priorities by diabetes type

| ***Impact statement*** | *Type 1 %, n=26* | *Type 2 %, n=49* | ***Impact statement*** |
|---|---|---|---|
| *My sleep is disturbed due to PDN* | 27.7 | 20.2 | *My sleep is disturbed due to PDN* |
| *I worry about keeping my physical fitness due to PDN* | 20.0 | 15.7 | *PDN causes me to have numb feet* |
| *PDN makes walking difficult* | 15.0 | 13.1 | *I am worried that my PDN will get worse in the future* |
| *PDN and balance problems lead me to fall over* | 14.2 | 12.9 | *PDN leads me to feel depressed* |
| *I get cramp more frequently than before I has PDN* | 13.8 | 12.2 | *I have to be careful walking due to my balance* |
| *PDN affects my ability to do every day jobs* | 13.5 | 11.8 | *I worry about keeping my physical fitness due to PDN* |
| *I have to check my feet regularly for possible injury* | 12.7 | 11.8 | *PDN makes it difficult to buy shoes that are comfortable* |
| *PDN gives me a sense of restless legs* | 12.3 | 11.6 | *I have lost confidence to be myself due to PDN* |
| *PDN leads me to get frustrated* | 9.6 | 9.6 | *PDN makes walking difficult* |
| *When PDN flares up I just want to be on my own* | 9.6 | 9.2 | *When PDN flares up I can be less tolerant to those around me* |

*6.11.8.3 Priority by pain intensity*

Respondents provided an average pain score (NRS) for the preceding week. Pain scores are subjective and do not offer a clear impartial way by which to categorise participants (Korff, Jensen and Karoly, 2000). The choice to use NRS provided categorical pain data that could be considered alongside the other subgroup categories explored. An initial process created three categories: mild (NRS 0-3), moderate (4-6) and severe pain (7-10) and resulted in a substantially larger sub-group with severe pain (mild n=15, moderate n=24 and severe n=39). Creating two categories for low pain (NRS 0-5) and high pain (6-10) created two, more balanced categories (low pain n=30, high pain n=48).

Irrespective of pain category, sleep remained the main priority (Table 27). The high pain subgroup reported greater emotional impacts – depression (16%), worry about fitness (13.5%), frustration (11.3%) and loss of confidence (10.8%) than the low pain subgroup. The high pain subgroup was the only respondent subgroup to prioritise an impact specifically relating to the subjective pain experience - *My feet look normal but I have this severe pain* (10.4%). The priorities of the low pain subgroup included sensory symptoms not explicitly painful - numb feet (16%), restless legs (15.3%), and functional impediments - the need to check feet regularly (11%).

Emotional concerns regarding the prognosis for PDN (15.3%), and the impact PDN might have on financial security (15%) remained in the low pain subgroup.

Table 27 - Priorities by pain category

| ***Impact statement*** | *High pain %, n=48* | *Low pain %, n=30* | ***Impact statement*** |
|---|---|---|---|
| *My sleep is disturbed due to PDN* | 19.4 | 26.0 | *My sleep is disturbed due to PDN* |
| *PDN makes walking difficult* | 17.7 | 16.0 | *PDN causes me to have numb feet* |
| *PDN leads me to feel depressed* | 16.0 | 15.3 | *I am worried that my PDN will get worse in the future* |
| *I worry about keeping my physical fitness due to PDN* | 13.5 | 15.3 | *PDN gives me a sense of restless legs* |
| *PDN causes me to have numb feet* | 11.9 | 15.0 | *I worry how our money will be affected because of PDN* |
| *PDN leads me to get frustrated* | 11.3 | 14.7 | *PDN makes it difficult to buy shoes that are comfortable* |
| *I have to be careful walking due to my balance* | 10.8 | 11.0 | *I have to check my feet regularly for possible injury* |
| *I have lost confidence to be myself due to PDN* | 10.8 | 9.0 | *PDN affects me as soon as I put my foot to the ground in the morning* |
| *My feet look normal but I have this severe pain* | 10.4 | 8.7 | *I have to be careful walking due to my balance* |
| *PDN affects my ability to do every day jobs* | 9.4 | 8.3 | *I get cramp more frequently than before I has PDN* |

*6.11.8.4 Priority by help seeking status*

There were noticeable similarities between the priorities of those who had sought help for PDN and those who had not (Table 28). Sleep disturbance (help seeking 25.9%, non-help seeking 31.3%) and worry about physical fitness (help seeking 18.9%, non-help seeking 16.7%) remained similar between these two groups and when compared to other sub-groups examined.

There were also differences. The respondents who sought help prioritised certain impacts to a greater extent than the respondents who did not. These impacts were walking (help seeking 21%, non-help seeking 6%), depression (help seeking 18%, non-help seeking 8%) and pain in the morning (help seeking 14%, non-help seeking 1.3%). These three impacts were not in the top 10 for respondents who had not sought help so have been added as extra lines in Table 28.

The impacts that occur in both subgroups have been colour coded to aid comparison in Table 28.

Table 28 - Priorities by help seeking behaviour

| ***Impact statement*** | *Help seeking %, n=37* | *Not help seeking %, n=24* | ***Impact statement*** |
|---|---|---|---|
| *My sleep is disturbed due to PDN* | 25.9 | 31.3 | *My sleep is disturbed due to PDN* |
| *PDN makes walking difficult* | 21.6 | 22.5 | *PDN causes me to have numb feet* |
| *I worry about keeping my physical fitness due to PDN* | 18.9 | 17.5 | *I am worried that my PDN will get worse in the future* |
| *PDN leads me to feel depressed* | 17.8 | 16.7 | *I worry about keeping my physical fitness due to PDN* |
| *PDN affects me as soon as I put my foot to the ground in the morning* | 14.6 | 16.3 | *I have to check my feet regularly for possible injury* |
| *PDN affects my ability to do every day jobs* | 14.1 | 15.8 | *I don't understand why I have PDN* |
| *PDN causes me to have numb feet* | 13.8 | 15.4 | *PDN gives me a sense of restless legs* |
| *PDN makes it difficult to buy shoes that are comfortable* | 13.5 | 14.2 | *I have lost confidence to be myself due to PDN* |
| *When PDN flares up I can be less tolerant to those around me* | 13.5 | 12.1 | *I have to be careful walking due to my balance* |
| *My overall quality of life is really affected by PDN* | 13.5 | 11.7 | *PDN makes it difficult to buy shoes that are comfortable* |
| | | 8.0 | *PDN leads me to feel depressed* |
| | | 6.0 | *PDN makes walking difficult* |
| | | 1.3 | *PDN affects me as soon as I put my foot to the ground in the morning* |

*6.11.8.5 Combining the subgroup priorities*

To explore priorities according to participant subgroup a table was created combining the top five priorities for each (Table 28). Six impacts were included in the top five priorities for at least three of the seven subgroups: sleep strategies, physical fitness, difficulty walking, experiencing numb feet and both depression and anxiety, related to PDN. The top-5 priorities from the sub-group who have not sought help for PDN are included in Table 29 for comparison, these are not dissimilar to the priorities of those who have sought help.

Table 29 - Top 5 priorities by sub-group

| ***Impact statement*** | Men (n=35) | Women (n=45) | Type 1 (n=26) | Type 2 (n=49) | High pain NRS 6-10 (n=48) | Low pain NRS 0-5 (n=30) | Help seeking (n=37) | Not help seeking (n=24) |
|---|---|---|---|---|---|---|---|---|
| *My sleep is disturbed due to PDN* | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| *I worry about keeping physical fitness due to PDN* | 4 | 2 | 2 | | 4 | | 3 | 4 |
| *PDN makes walking difficult* | 5 | 5 | 3 | | 2 | | 2 | |
| *PDN causes me to have numb feet* | 2 | | | 2 | 5 | 2 | | 2 |
| *I am worried that PDN will get worse in the future* | | 4 | | 3 | | 3 | | 3 |
| *PDN leads me to feel depressed* | | | | 4 | 3 | | 4 | |
| *I have to be careful walking due to my balance* | 3 | | | 5 | | | | |
| *PDN makes it difficult to buy shoes that are comfortable* | | 3 | | | | | | |
| *PDN and balance problems lead me to fall over* | | | 4 | | | | | |
| *I get cramp more frequently than before I has PDN* | | | 5 | | | | | |
| *PDN gives me a sense of restless legs* | | | | | | 4 | | |
| *I worry how money will be affected because of PDN* | | | | | | 5 | | |
| *PDN affects me as soon as I put my foot to the ground in the morning* | | | | | | | 5 | |
| *I have to check my feet regularly for possible injury* | | | | | | | | 5 |

NRS – Numerical rating scale; Green box – impacts prioritised; Numerals indicate order of top-5 priorities.

## *6.12 Discussion*

In this Internet survey a wide range of impacts, drawn from interviews with people with PDN, were presented to participants. The majority of impacts were identified by the survey respondents as present in their lives and affect these impacts had on quality of life ranged from small to large. People who used passive coping strategies experienced a greater negative impact on their quality of life, but active coping was not shown to be adaptive or to attenuate these impacts. Respondents were free to choose the impacts they would prioritise to manage better, and there were some consistent themes through the selection of priorities, irrespective of respondent subgrouping.

### *6.12.1 Frequency of impacts*

Fifty-four of the fifty-eight impact statements were individually recognised as being experienced by at least half the sample. These findings highlight the impacts of PDN on the individual as multi-faceted, wide-ranging and pervasive. Within the top-10 experienced impacts, were statements that described the subjective sensations of PDN (*My feet look normal but I have this severe pain, PDN causes me to have numb feet, PDN gives me a sense of restless legs*), but the

top-10 also included psychological impacts (*Worry that PDN will get worse in the future, PDN leads me to be frustrated*); social impacts (*PDN makes me less tolerant to those around me*); and functional impacts (*I have to check my feet regularly for possible injury, My sleep is disturbed, PDN makes walking more difficult*). The impact *PDN affects my ability to concentrate* could be considered social and/or functional.

*6.12.1.1 Impacts associated with neuropathy*

Four of these impacts – numb feet, restless legs, needing to check feet for damage and difficulty walking – were indicative of diabetic neuropathy, the prerequisite for developing PDN. It was not surprising that the majority of respondents had experience of these impacts, as some degree of impairment due to neuropathy would be expected, even without the experience of pain.

The most frequent impacts experienced highlight the disconnect between insensate neuropathy and neuropathic pain. Respondent's most frequent impact (94.8%) reflected the need to check their feet for injury because neuropathy had reduced the normal protective reactions to tissue damage. Engaging in regular injury surveillance, and finding no damage to account for the pain, was an impact experienced by 88.7% of respondents. This disconnect was a strong theme in the patient interview study (see Chapter 4 section 4.7) where participants increasingly kept their pain to themselves, and did not raise it with family and friends, because they could not explain the experience.

> *"You know what I mean, they're not gnarled and knotty, they look quite ordinary feet and yet they've got this most incredible pains." Lisa, F69.*

Pathologies often associated with persistent pain have a range of visibility to the observer. People with rheumatoid arthritis affecting their hands tend to have more obvious joint redness and deformity than those who do not have RA (Stone, 2009). People with Complex Regional Pain Syndrome often have a limb that is oedematous and red (McCabe and Blake, 2008). In contrast, other pathologies causing pain have minimal visibility to indicate their presence. For example, it is not possible to see lumbar or cervical disc pathologies without MRI scans (Suri *et al.*, 2014). Nerve conduction studies, a common objective measure of nerve function, can be within normal range in people with diabetic neuropathy (Horowitz, 2006). For all these clinical examples, there remains no clear relationship between objective signs and personal pain experience. Due to these inconsistencies, people with persistent pain problems have felt scepticism from others toward their experience (Smith and Osborn, 2007), even stigmatized as malingers (Slade, Molloy and Keating, 2009; Cohen *et al.*, 2011).

Concern about the opinion and reactions of others is a common experience when living with a persistent and private pain experience (Bunzli *et al.*, 2013; Cohen *et al.*, 2011; Smith and Osborn, 2007). A focus group study explored peoples' expectations of a pain clinic whilst they were waiting for a first assessment (Allcock, Elkan and Williams, 2007). The sample (n=18 in three focus groups) mainly experienced persistent spinal pain, with only one person with facial neuropathic pain. A strong theme of expectation for a diagnosis was found, as this would provide validation to society for the pain the person experienced. Diabetes is not uncommon and there is awareness amongst the general public that DM can cause numb feet, but the symptom of pain is under-recognised by the public and HCPs (Taylor-Stokes *et al.*, 2011).

Providing diagnostic labels has not been shown to have significant effects on health outcomes in FMS. FMS presents with a range of physical, mood and social impacts and patient response to the diagnosis can be variable, some finding it useful to validate their experience, others finding the label had negative connotations (Karjalainen *et al.*, 2009). A prospective study with 100 people, n=28 with an existing diagnosis of FMS and n=72 newly diagnosed with FMS were followed for 3 years (White *et al.*, 2002). Between group analysis found no meaningful differences in measures of symptom severity, FMS impact or health service usage between the groups from attribution of the FMS label. The study did not include any qualitative enquiry to establish whether the FMS label had altered the participants' quality of relationships and interactions with others in their social networks.

*6.12.1.2 Impacts associated with cognitions*

Psychologically, respondents were worried for their future with PDN, and frustrated by PDN. There have been few large-scale long-term epidemiological studies in PDN, to elucidate the natural history of the condition. Up-to-date reviews often cite the same few studies. Boulton *et al.* (1983) followed 39 patients with PDN over four years and found no change in pain ratings across that time (mean 5.3(SD2.0) to 5.6(SD2.5), non-significant); Benbow *et al.* (1994) followed 33 patients with follow up at mean 3.6 years, and found 88% improved in pain rating and only 12% worsened. In contrast Galer *et al.* (2000) in a retrospective survey (n=105) found 71% of respondents estimated their PDN had worsened since first onset, 15% rated it unchanged and 12% rated it as improved. The discrepancy of these conflicting data continues in current reviews (Coppini, 2016) and this leaves clinicians and patients uncertain for future changes in pain.

The impact phrase used in this survey – *PDN leads me to get frustrated* – was developed from the descriptions interview participants gave of limitations in day-to-day activity (Chapter 4 section 4.5.3). The survey development process asked EPRPs to sense check the statements but survey respondents may have had different interpretations, so caution is suggested. With this caveat, if we take frustration to relate to restrictions in the present, rather than due to past life

experiences or potential futures, there are links to other frequently experienced impacts. For example, there are clear links between frustration (impact experienced 89.7%), ability to concentrate (86%), reduced tolerance to those around me (84.5%), and difficulty walking (83.6%). Walking between tasks, even within the home is usually necessary to some degree. Pain has been described as an interfering perception, one that demands attention and so diverts attention away from competing tasks (Morley and Williams, 2015). Frustration can be thought of as opposition in the pursuit of an outcome; there is a sense of conflict in the language used. Some interview participants described less confrontational, more adaptive strategies to achieve what they planned day-to-day. These strategies included waiting for a day when pain was less severe to address the task, using walking aids to reduce worry of falling or hiring a wheelchair to extend the distance they could go from the car.

> *"You know the things and the places will always be there, they will be there the next day so if you don't achieve something today there is always tomorrow." Joan, F57.*

The self-perception of problem solving ability and the impact of worrying about pain has been explored with people with chronic pain (de Vlieger, Crombez and Eccleston, 2006). Using the Problem-Solving Inventory, a measure of participant's perception of their own behaviours related to problem-solving, pain clinic patients (n=185, 54% LBP) had a mean score of 91.86 (SD25.43), which was not significantly different when compared to a community cohort (mean 90.46 (SD24.36). Problem solving behaviours did not contribute to regression models for pain or pain-related disability. Reduced confidence in problem solving did have a positive correlation with depression ($r=0.24$, $p<0.01$) and pain-related disability ($r=0.16$, $p<0.01$). Study participants also completed the Worrying Domains Questionnaire. Previous research had used cluster analysis to define five domains of worry: 1) relationships, 2) lack of confidence, 3) aimless future, 4) work incompetence and 5) finances. The total Worrying Domains Questionnaire score was not significantly different between the two groups (pain clinic mean 25.75 (SD19.78); community cohort 24.85 (SD18.61)). Worrying and catastrophizing about pain did contribute toward models for depression ($\beta=0.35$, $p<0.005$ and $\beta=0.29$, $p<0.005$, respectively).

Neither the interview study (Chapter 4) nor this survey study were designed to explore whether adaptive problem solving, or less confrontational approaches to day-to-day frustrations had any bearing on quality of life. Reflecting on the patient interviews suggests that those who described active problem solving and adaptations in the presence of PDN, were more optimistic describing less impact on their quality of life. It would be interesting to quantify how people with PDN consider their own problem solving abilities using specific outcome measures and an appropriately powered sample size.

The issue of worrying and catastrophizing about pain returns to the first impact discussed in this section, that respondents were frequently concerned about their future prognosis with PDN. The issue of frustration, with the connotation of day-to-day restrictions of agency also returns to the philosophical underpinnings of common psychological interventions for pain – ACT and CBT (see Chapter 1 section 1.5.2). ACT particularly focuses on reducing the use of behaviours and thinking styles that involve resistance, rather, emphasising behavioural and psychological flexibility (McCracken and Vowles, 2014).

*6.12.1.3 Impacts associated with function*

Sleep was identified as the third most frequent impact (91.8%). This is reflective of the known affect PDN has on sleep from quantitative research (Zelman, Brandenburg and Gore, 2006), as well as other neuropathic pain conditions such as MS (Braley, 2015), and non-specific wide spread pain conditions (McBeth *et al.*, 2015). Reduced sleep quality impairs the person's resilience to cope with living with persistent health problems (Sivertsen *et al.*, 2015).

When effective, analgesic medication for pain can reduce the impacts of a pain condition. For example, Hoffman *et al.* (2010) in a study with n=401 people with PDN, found a 30-39% reduction in pain was associated with a mean reduction of -2 points (on a 0-10 scale) interference in sleep quality. Using a different metric for pain reduction they found if the pain reduced from 'severe' to 'moderate' intensity, sleep interference reduced by a mean -5 points (BPI). Whether such changes are meaningful to the person are unknown, studies to define the minimum clinically important difference have tended to focus on pain reduction, rather than pain interference reduction.

Nonetheless, the relationships between sleep, pain and cognitive variables are complex. Sleep disturbance and pain are suggested to have bidirectional associations whereby one symptom negatively affects the other (Sivertsen *et al.*, 2015; Finan, Goodin and Smith, 2013). Although inter-related, the evidence suggests the relationship is weighted toward sleep-related cognitions having a larger impact on sleep, than pain severity (McBeth *et al.*, 2015). For PDN an association has been found between worsening sleep quality and both increased pain ($r=0.40$ $p<0.001$) and increased symptoms of depression ($r=0.30$, $p<0.001$). Sleep disturbance was shown to mediate the effect of pain on depression scores from $r=0.34$ to $r=0.29$ (both $p<0.001$) (Hughes *et al.*, 2016).

The rationale for the use of Amitriptyline for persistent pain can be based on sedative side effects. Patients do not report less pain, but that they can cope better, having slept better. This finding was present in both patient and clinician interview results.

*"…if the pain is worst at night that would push me more towards Amitriptyline, because Amitriptyline tends to cause a bit of sedation and therefore actually helps people with sleep." Diabetes Consultant 1.*

Walking was another day-to-day functional act impeded by PDN. Eighty-three per cent of respondents experienced walking issues because of PDN. This finding was consistent with other quantitative research that found walking and sleep to be most interfered with by PDN (BPI subscale 4.6-5.6/10 (Tölle, Xu and Sadosky, 2006; Galer, Gianas and Jensen, 2000; Hoffman *et al.*, 2010)). Seventeen per cent of survey respondents did not experience issues from PDN when walking. A number of interview participants described being 'aware' of their feet, but not 'in pain' when walking (Chapter 4 section 4.5.4). Subjective appraisal of meaning and context can have the effect of changing the unpleasantness of an experience (Bartolo *et al.*, 2013; Moseley and Arntz, 2007).

*6.12.1.4 Impacts least frequently experienced*

The least experienced impact of PDN was contemplation of suicide (not experienced by 70.7%). This result was a relative outlier, as the second least experienced impact - *PDN leads me to have headaches* – was not experienced by 53.4% of respondents. This result does however imply that 30% of people with PDN had suicidal thoughts at some time. This would be a significant number of people if representative of the UK population with PDN. A review of suicide in a range of chronic pain conditions found people with persistent pain were more than twice as likely to commit suicide than those without pain, with lifetime prevalence found to be 5-14% (Tang and Crane, 2006). Tang and Crane (2006) identified eight risk factors for suicide, these included pain-related sleep-onset insomnia, pain catastrophizing, helplessness in the face of pain and reduced problem-solving ability. These issues were all been identified by the survey respondents, and in the wider population with PDN (Zelman, Brandenburg and Gore, 2006; Geelen *et al.*, 2016; Sullivan, Lynch and Clark, 2005).

Other less frequently experienced impacts have associations with central sensitisation as a predominant pain mechanism. Headaches are not part of the diagnostic criteria for PDN (Peltier, Goutman and Callaghan, 2014), yet 47% of respondents associated them with PDN. Headaches, particularly involving light sensitivity, have been suggested part of the symptom profile for pain with predominantly central mechanism (Nijs *et al.* 2010). Similarly, PDN affecting memory was identified by 50% of respondents. Cognitive decline (Biessels, Deary and Ryan, 2008) and prolonged stress over the life span (Chrousos, 2009) have been associated with diabetes and can manifest as problems with reduced short-term memory.

Some impacts, which appear similar, were present in both high frequency and low frequency analysis. *Worry about PDN into the future* (93.4%), presented as a general concern for future prognosis, and within the least frequent impacts – *Worry about going out of the house* (44%) and *Worry about how money will be affected* (45%). Similarly, *When PDN flares I can be less tolerant to those around me* (84.5%) is comparable to *My PDN affects my close family* (44.8%).

The occurrence of similar impacts in both high and low frequency analysis could be explained by a number of factors: 1) respondents selected the rating for each impact considering their own situation - if retired and not dependent upon work for income, then selecting an impact related to future earnings would be less likely; 2) all impact statements were derived from interviews where the participants used their own words to describe the impacts of PDN. The phrasing of impact statements was kept faithful to the language used in these interviews. Had the response rate been sufficient, PCA would have collapsed the 58 individual impacts to a reduced number of indices for discussion.

*6.12.2 Severity of impacts*

It was interesting to note the top-10 most severe impacts of PDN (Table 18) did not include any that described the subjective pain experienced with PDN. Rather, the impacts in Table 18 may be classed as psychological (worry, frustration), social (other peoples' opinions, social life) and functional (sleep, general activities, physical activity). The sensory impacts of cramp and numbness, reported in this study, are common with non-painful diabetic neuropathy (Peltier, Goutman and Callaghan, 2014). Headaches had not previously been linked with PDN but have with central pain states (Nijs, Van Houdenhove and Oostendorp, 2010), yet headaches related to PDN were experienced by 47% of the respondents and rated as having a severe impact on quality of life when present (74.5%).

These results were plotted in graphical form in Figure 19. The least rated impact for severity (*PDN and balance problems lead me to fall over)* was rated 1 or 2/4 (no or minimal) for impact on quality of life by 52.9% of respondents, therefore rated as 3 or 4/4 (moderate or large) by 47% of respondents. Although this discussion dichotomizes the results to the great and least impact on respondent quality of life, the reality is not black and white.

*6.12.2.1 Impacts affecting quality of life the most*

The impact on quality of life rated as most severe by participants was worry about PDN worsening in the future. The natural history of PDN is uncertain from the few longer-term studies available (see section 6.12.1.2 for details) meaning that it is not possible to allay patient's worry about future prognosis and impact.

The impact rated second for severity, related to the perception of others. The discussion in section 6.12.1.1 remains relevant when considering impact severity as well as frequency.

Reductions in sleep quality are known to have negative associations with quality of life (McBeth *et al.*, 2015; Finan, Goodin and Smith, 2013) and to increase the risk of depression (Hughes *et al.*, 2016) and suicide (Tang and Crane, 2006), the discussion in section 6.12.1.3 remains relevant when considering impact severity as well as frequency.

Three impacts (*PDN affects a wide range of activity, I have reduced my physical activity due to PDN,* and *PDN affects my social life*) may all be considered measures of engagement with the society that surrounds the person. A reduction in life engagement is common in other persistent pain conditions but is not linear to the intensity of pain experienced; rather, engagement can be mediated by cognitive factors such as fear-avoidance and catastrophizing (Vlaeyen and Linton, 2000; Wideman *et al.*, 2013). Models of fear/avoidance (Vlaeyen & Linton 2000) highlight that withdrawal from life engagement will likely lead to loss of fitness and increased depression, which in turn increase the pain experience. This vicious circle can be very difficult to break, but has clear links to the impact respondents rated most severe – the prognosis of PDN.

Restrictions to daily activity, physical activity and social life are possible sub-issues that contribute to the impact of *PDN leads me to get frustrated* (75%). This survey study has shown frustration to be frequent as well as severe in the effect it has on quality of life. Please refer back to section 6.12.1.2 for more discussion on the role of frustration in PDN.

*6.12.2.2 Impacts affecting quality of life least*

It was surprising *PDN hurts so much it brings tears to my eyes* was rated as having no, or minimal impact on their quality of life by 41.7% of the sample. The wording of the impact statement came from an interview quote and it is possible that different wording would have led to different results. The absence of pain from the most severe impacts and its presence in the least severe impacts, highlights focus on pain reduction *per se*, may not be the patient's priority for PDN management.

Similarly, *My skin is sensitive to the lightest touch*, as a description of allodynia, one of the clinical hallmarks of neuropathic pain and central sensitisation (Smith *et al.*, 2012), was rated as having little impact on life quality by 43.1% of respondents. Interview participants (Chapter 4) often described the sensory irritation from the bed sheets contributing to their disturbed sleep. Although this impact was within the 10 least severe impacts the respondents were nearly equally divided regarding the severity of the impact.

Three impacts may be considered together - *PDN makes me feel embarrassed (44.4%), I don't understand why I have PDN (47.1%),* and *PDN and balance problems lead me to fall over (52.9%)*. The issue of understanding the causes for PDN would seem to have links to the difficulty interview participants and survey respondents had for explaining their pain experience with little sign of damage. The risk of falls increases with neuropathy and falling could be embarrassing. Interview participants described other people assuming they were drunk if they fell in the street.

Without the benefit of statistical models the planned PCA would have provided, it appears that impacts rated most severe on quality of life may be considered higher-level descriptions of problems, and those rated less severe are more specific examples of the higher-level problems. If an impact statement had direct resonance to the respondent's experience, they would select the specific example, if not, the respondent may choose an impact statement more global in implication. For example: *It bothers me that other people can't see I have this problem* is a high-level impact statement, that could contain a number of sub-impacts – *PDN and balance problems lead me to fall over, I don't understand why I have PDN,* which may or may not be of direct relevance to a survey respondent.

*6.12.3 Impacts are associated with other diabetes complications and sociodemographic variables*

The introduction presented sociodemographic risk factors associated with the development of DM (Chapter 1, section 1.1.5). Chapter 1 also described the co-morbidities associated with diabetes, and how these co-morbidities may be considered complications in their own right. This survey did not ask details of social variables, such as postcode, or presence of common co-morbidities, such as cardiovascular disease or nephropathy. Nevertheless, all respondents will have a unique profile of these social and clinical variables, and these variables necessarily affect one another in a complex manner.

An example of such complexity can be seen in the Norwegian HUNT3 study (Tomasdottir *et al.*, 2013, 2015). In HUNT3 health data were collected from an ethnically homogenous and socially equitable region. The researchers gathered self-report data on a range of health and sociodemographic variables. They recorded the prevalence of twenty-one chronic health conditions, including DM, and twelve factors associated with stress responses (for example, blood pressure, heart rate, C-reactive protein and cholesterol levels). Tomasdottir *et al.* (2013) examined the clustering of diseases across the sample population. They found that if DM were considered the index disease, 9% (55/607) of people would have no other comorbidities and 51% (313/607) would have three or more comorbidities. In comparison, for people with persistent LBP as the index condition, 23% (1825/7927) had no other comorbidity and 27% (2145/7927) had three or more comorbidities.

Respondents in HUNT3 were also asked one question on the quality of their childhood (5 points, very good to very difficult). A general trend toward increasing prevalence of chronic health conditions was found as the self-rating of childhood experience worsened. For those with a 'very good' childhood, 27% had no health conditions, and 22% had three or more chronic health conditions. For those with a 'very difficult' childhood, less than 5% had no health conditions and 57% had more than three health conditions (OR 1.90 (CI 1.79 to 2.02)). Diabetes prevalence increased from 4% (very good childhood) to 7% (very difficult childhood) (Tomasdottir *et al.*, 2013).

Tomasdottir *et al.* (2015) put forward the hypothesis that difficult family upbringing as well as other sociodemographic variables and life experiences, can contribute to allostatic overload. Allostasis is where multiple systems compete to find homeostatic balance, but these systems are not in isolation and so affect one another (Chrousos, 2009; Tsigos and Chrousos, 2002). With sustained stress from life and social factors the resilience of bodily systems maybe so challenged that chronic physical and mental health problems develop.

Measures of social deprivation have been found as risk factors for developing PDN in people with T1DM (Anderson *et al.*, 2014). Anderson *et al.* (2014) surveyed 1621 medical records for patients with T1DM who were receiving treatment for neuropathic pain (n=280). Records included Townsend Deprivation Index (TDI) data, a measure that counts unemployment, non-car ownership, non-house ownership and household overcrowding as variables for social deprivation. The TDI ranges from -5 to +7, with higher score indicating more social deprivation. There were significant differences in TDI between those with neuropathic pain to those without. Patients were more likely to score TDI ≥ 1 (34.3% vs. 27.1%, $p<0.001$). Multi-variant analysis showed each unit increase of TDI was associated with 11% increase in the odds ratio to require pharmacological management of neuropathic pain (OR 1.11 (CI 1.05 to 1.17), $p<0.001$). This was independent of age, sex, HbA1c, BMI and blood pressure.

The diabetes clinicians interviewed were keen to stress that patients who had developed microvascular complications, would inevitably also present with macrovascular complications (peripheral and cardiac vascular disease, nephropathy, other mobility restrictions from neuropathy). They highlighted that any potential interventions for PDN would need to consider these other issues in its design. The complications and co-morbidities are particularly relevant to exercise prescription and the risk to insensate feet. They are also relevant because many of these non-PDN issues are associated with psychological impacts, therefore any psychological intervention needs to be specific to the impact of PDN and possibly applicable to other causes of distress.

For PDN, which has impacts both wide-ranging and interconnected, it is not surprising a mono-modal approach to management thorough analgesic medication has been less than successful. As outlined earlier, the response statistics (NNTs) for the recommended medications are low, and this survey now demonstrates that people with PDN do not necessarily prioritise pain reduction. With common impact co-occurrence, it may be appropriate to consider more multi-modal approaches for overall management of PDN, within the context of common diabetic co-morbidities.

*6.12.4 Coping with PDN*

In comparison to the population with PHN (Haythornthwaite *et al.*, 2003), the survey respondents reported engaging in higher levels of active coping strategies. Reinterpretation of symptoms, Activity engagement and Ignoring symptoms, all had large effect sizes of 1.0-1.35 (Cohen's *d*). Survey respondents also reported using passive coping strategies to a greater extent than the PHN cohort. Catastrophizing was highest in the survey sample, with the largest effect size ($d$=1.37), similarly Praying was higher in the survey cohort than the PHN cohort with a medium effect size ($d$=0.48).

Examining the correlation between coping strategies and impacts of PDN there were strong associations between passive coping strategies and the impact of PDN. This association was present whether the number of impacts (r=0.537), the severity of impacts (r=0.587), or the total score of impacts (r=0.619, all $p<0.001$) was considered. If respondents employed passive coping strategies, they reported a greater impact of PDN on their lives.

However, engagement in active coping strategies did not have an association with the impact of PDN, whether number of impacts (r=0.235), severity of impacts (r=0.019) or total score (r=0.155, all non-significant) were considered. It would seem employing active strategies such as activity, diverting attention and ignoring sensations, do not necessarily mitigate the experienced impact of PDN.

*6.12.4.1 Current models for coping with persistent pain*

Coping with pain is a broad subject area and there are multiple theoretical models currently used for conceptualising the cognitive and behavioural processes involved. Consequently, there are many outcome measures for aspects of these theoretical models. This study used the CSQ as an outcome measure that quantified behaviours on the continuum between active and passive coping. For there to be such an asymmetric relationship between patients' coping styles and PDN impacts suggests, either active strategies really do have no benefit to PDN or, the constructs of active coping captured by the PCS questionnaire were not appropriate for this population.

There may be more nuanced approaches to coping that should be considered. A recent study examined pain-related coping using the Brief Pain Coping Inventory-2 (BPCI-2), an outcome measure containing two domains: *traditional pain management* (pacing, exercise, positive self-statements, distraction) and *psychological flexibility* (acceptance of pain/distress, present moment focus and engagement in valued activity) (Vowles *et al.*, 2014). This cross-sectional study (n=324, community pain service, 50% LBP) found no association between use of traditional pain management approaches, and measures of patient function (-0.09 to 0.08, non-significant). There was greater correlation between subscales measuring psychological flexibility and patient function (-0.3 to -0.45, all $p<0.005$). The strategies Vowels *et al.* (2014) defined as *Traditional pain management strategies* were consistent with those defined as Active Coping by the CSQ.

The study by Vowles *et al.* (2014) supported previous work trying to disentangle coping with pain, from acceptance of pain (McCracken and Eccleston, 2003; Turner, Jensen and Romano, 2000). McCracken & Eccleston (2003) found measures of coping were weakly associated with patient function, whereas acceptance was more strongly associated with greater activity, better work status and less depression, anxiety and disability. Turner *et al.* (2000) found patient coping was associated with physical function but not depressed mood; catastrophizing was associated with depression but not physical function, and measures of patient belief were associated with both physical function and depression. Creating an encompassing model of these wide-ranging constructs is beyond the scope and aim of this thesis, but there are aspects from these cited studies, and other literature that are relevant.

Chapter 1 outlined the neurobiology of PDN. A common feature of neuropathic pain is spontaneous exacerbations. Previous research found people with neuropathic pain did not find strategies taught by musculoskeletal PMPs, such as pacing, to be useful in managing spontaneous pain exacerbations (Daniel *et al.*, 2007, 2015). The results of the current survey suggested using active coping strategies, those frequently advised by PMPs, do not mitigate the impact of PDN.

There is little current evidence exploring psychological approaches to managing PDN (Chapter 2), but it maybe promotion of acceptance and psychological flexibility could be beneficial for this population. In their review of notions related to quality of life, Barcaccia *et al.* (2013) note other authors have considered QOL as "*the gap between what a person is capable of doing and being, and what they would like to do and be; in essence it is the gap between capability reality and expectations*". If people were able to engage in valued activities despite pain, this may help to reduce the severity of impacts identified in this study (Table 18). If people could engage in the functions and social activities identified, they may rate their quality of life as improved, whilst also providing physical loading and stress to their tissues that may offset ulceration (Chapter 5, section 5.6.2).

*6.12.5 Priorities for management*

During the survey design process literature searches were completed to find precedents for scoring and analysing patient priorities in managing disease impacts. Studies were located that investigated priorities of people with RA to find the impacts most important for improving with medication strategies (Sanderson *et al.*, 2010). Rheumatology patients present with a range of issues that the spectrum of anti-inflammatory medication options does not adequately address. Inflammatory pain, such as that experienced in RA, has specific mechanisms that are distinct from neuropathic mechanisms in PDN, so research findings may be informative but cannot be assumed to transpose to PDN. The analytic approach to calculate patient priority scores used in the current study was based on the method used by Sanderson *et al.* (2010a).

Despite examining a variety of subgroups within the survey sample, certain impacts were consistently prioritised by respondents. The top six impacts that respondent subgroups consistently wanted help to manage were: sleep disturbance, worry about physical fitness, difficulty walking, numb feet, anxiety for the future and depression. The functional nature of these priorities has similarities and differences to the findings of Schneider *et al.* (2014). Schneider at al. (2014) had asked patients with PDN to select which areas of interference due to PDN they wanted pain treatment to improve. The areas of interference were the subscales from the BPI. They found increased activity levels (29.3%, CI 27.5 to 31%) and walking ability (24.4%, CI 22.8 to 26.1%) were the highest priorities, with sleep rated third (14.7%, CI not specified). In contrast this survey found sleep problems were consistently the top priority (21.9%), irrespective of patient subgroup. Worry about physical fitness (14.1%) and difficulty walking (12.1%) could be considered analogous to the BPI interference scales of increasing activity and walking.

It is notable that respondents did not highly prioritise the pain of painful neuropathy. Respondents in the high pain category subgroup rated *My feet look normal but I have this severe pain* as their 9$^{th}$ treatment priority (10.4%). *PDN affects me as soon as I put my foot to the ground in the morning* was within the top-10 priorities for respondents with low pain (9%) and those who had sought help (14%). It was surprising to find subjective pain experiences were relatively low in priority compared to functional and cognitive impacts of PDN, since pain severity is the focus of the treatment guidelines and the majority of current research on PDN management.

Pharmacology research has investigated sleep disturbance and fatigue in PDN specifically, using the SF36 vitality sub-score as a measure of fatigue (Fishbain *et al.*, 2009). Baseline vitality scores were found to be lower for the cohort with DM/PDN (mean 47.7(SD18.8)), than the population with DM alone (55.7(SD21.6)) or the healthy population (59.9(SD22.1)). Treatment with Duloxetine compared to placebo reduced pain severity (mean -2.7(SD2.3)), night pain (-2.9(SD2.5)), and sleep interference (-3.1(SD3.0)), and increased vitality (8.7(SD18.6), all $p \leq 0.001$).

A path analysis was conducted and it was concluded that improvements in vitality were primarily due to reduced pain. The study does not highlight that Duloxetine, a selective serotonin-norepinephrine reuptake inhibitor, is a centrally acting anti-depressant. No data were provided on depression at baseline or follow up points, and depression did not appear to be considered within the pathway analysis. The issue of Duloxetine as an analgesic and antidepressant has been addressed in a post-hoc analysis of study data, where patients with PDN and notable depression were found to respond preferentially to Duloxetine compared to Pregabalin (anti-epileptic medication) (Ziegler *et al.*, 2014).

The diabetes clinicians were clear they understood PDN had a range of impacts on the person, in terms of mood, sleep and social function, yet beyond medication they had few management options. Once medication strategies were exhausted they had little to offer the person. The pain clinicians interviewed during the study presented in Chapter 5 were clear they felt an ethical obligation to ensure all potential analgesic treatments had been explored (see chapter 5, section 5.4.1), and there were possible strategies to manage impacts of pain depending on the patients' presentation, beyond medication.

This study highlighted that people have a range of priorities beyond just pain relief and, when considered with the results of the patient interview study, have a range of perspectives on non-pharmacological strategies. It would seem appropriate that clinical consultations are sufficiently open to allow these priorities and perspectives to be articulated between clinician and patient, and appropriate treatment decisions made. The treatment decisions formulated in collaboration between clinician and patient may still focus on pain reduction, but where pain was not the patient priority, or medication options exhausted, other treatment options which do match their expectations and priorities need considering.

## *6.13 Limitations*

### *6.13.1 Sample bias*

Sample bias is the error between sample population and whole population data, which can occur when the sample does not adequately represent the population. This survey required sampling a population who were homogenous, in that they all experienced symptoms consistent with PDN but were heterogeneous for other sociodemographic and clinical variables.

The characteristics of the survey population had similarities to the interview study presented in Chapter 4. The survey sample had a similar percentage of sex split (male 45%, compared to 47%) and types of diabetes (T2DM 63%, compared to 56%). The respondents were slightly younger (survey population mean age 57 years, compared to interview study mean 62.5 years, p=0.109), and the age range in both studies extended from 24 to 86 years. The survey

respondents were less likely to be retired (46% compared to 86%) and had been diagnosed with diabetes and PDN for less time than the interview sample (diabetes - mean 17.8(SD13.7) years, compared to mean 23.5(SD17.8) years, p=0.04; PDN - mean 7.3(SD6.3) years, compared to 10.3(SD7.3) years, p=0.02). In terms of age and duration with diabetes and PDN, the samples are representative of the wider UK population. To minimise non-completion of the study, information about comorbidities and DM complications were not requested so the full clinical profile of survey respondents is not known.

The statements of impact used in this survey were derived from an ethnically homogenous population that could lead to bias in results and conclusions if translated to the entire diabetes population. In an attempt to mitigate this bias, this survey allowed respondents to add their own experience of the impact of PDN as free text response, if the statements presented did not encompass their experience.

The free text comments added by respondents required creation of three new codes to encompass the impacts they described (see section 6.11.4). These codes were subsumed within the theme structure developed in Chapter 4 and did not lead to any significant alterations the theme structure. However, the survey sample was again predominantly White British (90%) and caution should be exercised when extrapolating the results of this survey to populations with different sociocultural make up.

*6.13.2 Sample size*

A sample size was specified to meet requirements for conducting a PCA, but this sample size was not met. The results and discussion for impact frequency and severity are based on data for all 58 impacts, and not a reduced number of indices PCA may have provided. The subgroup analysis of respondent priorities further reduced the sample size present within each sub-group. These results should be considered preliminary and require further research using different survey distribution options to increase the response and consequent sample size and sociodemographic variety.

*6.13.3 Priorities chosen without contingencies*

In asking respondents to prioritise the impacts they wanted help with, each impact was considered a separate entity or issue. This survey did not allow respondents the option to suggest certain priorities maybe dependent or contingent on other variables. For instance, loss of physical fitness and walking ability were rated as priorities by five of the seven subgroups examined. Improving these aspects of physical function maybe contingent on more manageable pain levels.

*6.14 Conclusions*

This study has taken impacts drawn from qualitative research and presented them within an Internet survey. This has allowed the impacts of PDN described by interview participants to be validated and endorsed (or not) by a larger population. The individual impacts presented were experienced by at least half of the respondent sample and were often rated as having a moderate to large impact on quality of life. The impact statements that referred to the subjective experience of PDN were not as highly rated as might be expected, whereas functional, mood and social impacts were rated as having the most impact on quality of life. Similarly, when asked to select which impacts were most important to manage better, respondents selected sleep, daily function, worry and depression related to PDN over the subjective experience of pain.

Passive coping strategies had strong association with more frequent and more severe impact ratings, but active coping strategies were not associated with reduction of impact. The strategies required to meet patient priorities will be the focus of the next chapter. It will explore whether or not the priorities identified in this study can be mapped to existing strategies to aid in their management.

*This chapter has described an Internet survey to explore the priorities people with PDN had for improved management. The options presented were based on the interview study in Chapter 4. The following chapter will consider the top six priorities in detail, examining the clinical implication of each and directions for further research.*

# Chapter 7 – Patient priorities: clinical and research implications

*The previous chapter detailed the results of an Internet survey that asked respondents which impacts of PDN they would prioritise for better management strategies. When the top 5 priorities for the seven subgroups were examined, there were six specific impacts consistently prioritised. This chapter will present a discussion of the management strategies currently in existence for these six impacts that may be of benefit to people with PDN. It will consider how these potential interventions could be delivered to help people cope with these priority impacts and make suggestions for further research within each section.*

This thesis aimed to examine whether physical and psychological strategies from PMPs would be considered relevant and acceptable to people with PDN and, if so, how they may need to be refined for this specific population. Figure 20 - Evidence synthesis, represents the current situation: DM and associated complications are increasing in prevalence, current PDN management focusses primarily on medication with minimal use of specialist pain management strategies. The new knowledge developed from the studies within this thesis can now be considered alongside research from existing pain management and other chronic disease management approaches. This combined knowledge will inform the potential viability of adjunctive management strategies for PDN. This process will also highlight where further research is required.

The survey presented in Chapter 6 found six priorities were commonly rated as important by respondents. There was some consistency in these even when subgroups of respondents were examined. Each of these priorities will be considered in the following sections detailing the evidence for management and suggestions for further research as required.

Although the impacts identified in Chapter 6 had commonalities between subgroups they were not uniform. The diabetic specialist and primary care clinicians interviewed (see Chapter 5) were clear that individual patients presented with differing profiles of clinical issues. The interviews with both clinicians and patients suggest the impacts associated with PDN do not sit with any one member of the diabetes multi-disciplinary team (MDT), or exclusively in either primary or secondary care. Rather, it is the responsibility of the clinician to ensure their consultations allow the person to raise issues which are of most importance to them. It is then the responsibility of the clinician to either suggest strategies to manage that impact, or to know how to refer to the appropriate clinician or service. The suggestions in the following sections could be used by individual clinicians, as well as forming components of a MDT PDN intervention.

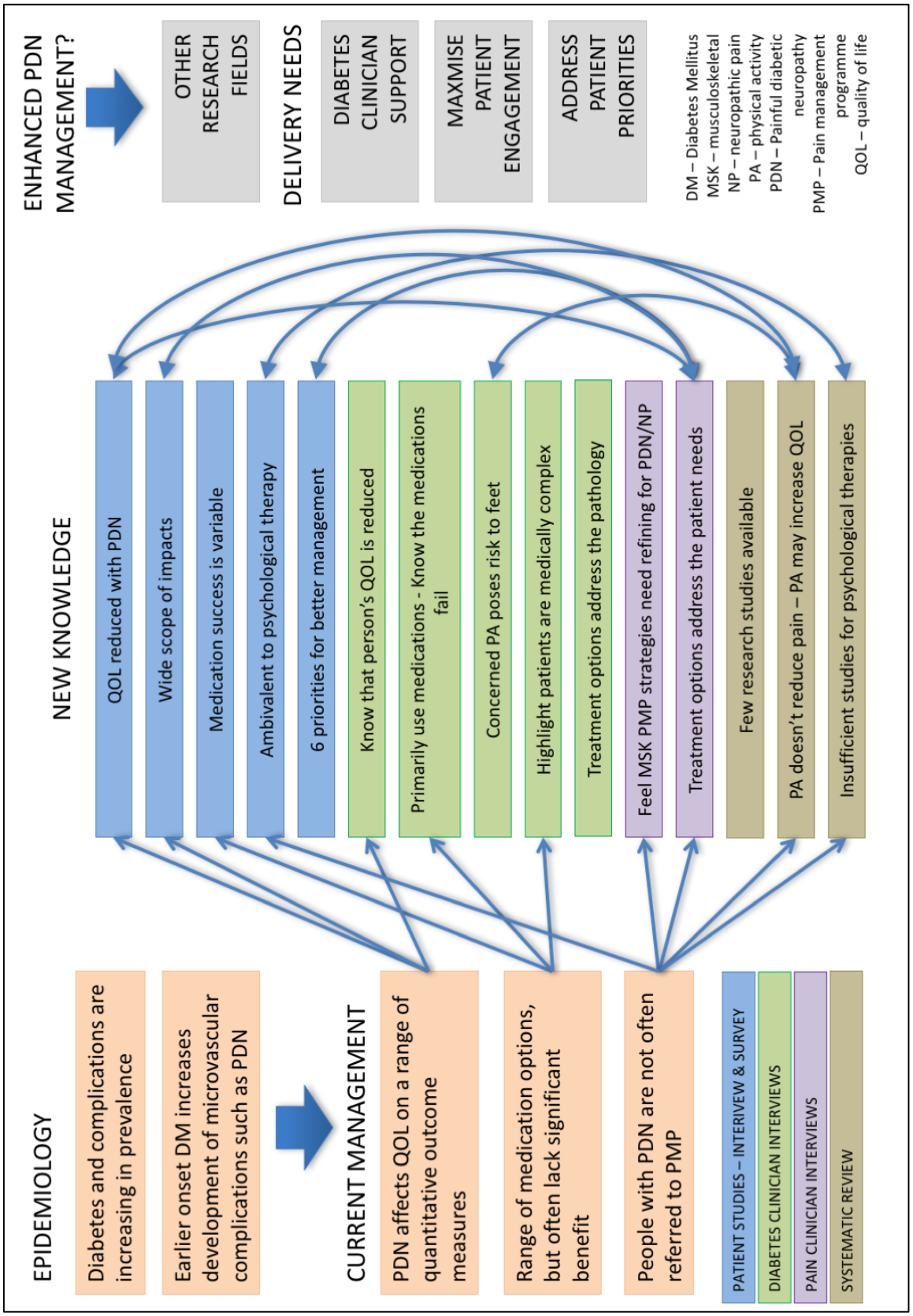



Figure 20 - Evidence synthesis

The following sections will now describe each impact prioritised by respondents in the Internet survey and consider the clinical and research implications of each.

*7.1 My sleep is disturbed due to PDN*

Nearly all patient interview participants described diminished sleep quality, or consequent day-to-day difficulties resulting from lack of sleep. Clinicians would often consider using Amitriptyline due to its sedative side effects, but excessive drowsiness the following day was a common complaint from patients. No interviewees reported receiving any advice about sleep strategies.

Sleep disturbance due to PDN was the top management priority for all sub-groups examined. Pain and sleep disturbance have a close relationship. Recent literature reviews suggest that while pain can affect measures of sleep adequacy and quality, the stronger relationship is for disturbed sleep to worsen the pain experience (Sivertsen *et al.*, 2015; Tang, 2009). While pain and insomnia maybe precipitated at the same time, the impact pain has on sleep quality reduces over time, but the effect cognitive and behavioural factors have on pain appear more enduring (Tang, 2009).

Existing CBT PMPs often include sleep hygiene strategies education, but there is clearly less content specific to sleep than CBT for Insomnia (CBT-I) programmes. CBT-I has greater content on specific sleep strategies (sleep restriction), stimulus control approaches (sleep when sleepy not tired, regular get up time, increase the association between bed and sleep) and paradoxical intention (reduce the effort to sleep and so reduce performance anxiety) (Edinger and Means, 2005; Trauer *et al.*, 2015). PMPs, where the focus is on managing pain, use single-item self-report measures or do not routinely report sleep outcomes, therefore data are limited on the effect standard PMPs have on sleep. A systematic review by Tang (2009), including studies specifically investigating CBT for insomnia with people in pain (n=3 studies), found some positive benefits, with improved sleep efficiency (Cohen's *d* effect sizes 1.0-2.0) and reduced sleep onset latency (effect size 0.9-2.1). All three studies included found no benefit for participants' pain ratings.

In comparison, CBT-I programmes have a greater evidence base for improving measures of insomnia in people with a primary sleep disorder. A systematic review of CBT for primary insomnia (n=19 studies) concluded that measures of sleep quality increased by clinically and statistically significant levels post-treatment, when compared against no active treatment (sleep onset reduced by 19 minutes (CI -23.9 to -14.1), and sleep efficiency (time asleep/time in bed as %) increased by 9.9% (CI 8.1 to 11.7) (Trauer *et al.*, 2015). The authors note their eligibility criteria excluded studies that included common medical comorbidities of insomnia, so their results may only be applicable to primary insomnia.

Programmes based on ACT have also addressed insomnia. ACT has a different focus than CBT, promoting strategies to address metacognitive processes (thinking about thinking) rather than challenging the cognitions themselves. A model of ACT for insomnia makes a distinction between primary arousal – expectations about sleep, worry about the daytime consequences of reduced sleep, and secondary arousal – the cognitive bias toward certain thoughts, rigidity in thinking and attachment to these thoughts (Ong, Ulmer and Manber, 2012). Ong, Ulmer and Manber (2012) suggest four stances that can be more adaptive: balance (allowing sleepiness to guide bed time), flexibility (sleep intentions change with context), equanimity (patience and not striving for sleep) and commitment to values (focus on important aspects of life despite a range of thoughts and emotions). A recent case series, non-randomised trial examined ACT for insomnia in people who had not responded to CBT-I interventions (Hertenstein *et al.*, 2014). The researchers found insomnia-related quality of life improved significantly (p=0.017) and was sustained at three-month follow up. This preliminary study was small scale (n=11) and did not have an active control group, so results cannot be assigned to the intervention with certainty.

### *7.1.1 Clinical implications*

Sleep was the top priority for survey respondents suggesting that management of sleep issues associated with PDN requires clinical strategies. Clinicians who are involved in the management of PDN need to have skills to advise patients on sleep strategies. It may be appropriate to base this advice on CBT-I principles, but further research specifically using CBT-I in neuropathic pain conditions is required. With the aim for the patient requiring as few appointments as possible, there is no reason why members of the current diabetes MDT could not be trained to provide appropriate sleep advice. It may also be appropriate to bring other clinicians into the MDT team, specifically Occupational Therapists who may have more specific experiences discussing and advising sleep strategies.

The issue of MDT skill mix, or, ensuring the patient sees the right clinician for help with the impacts of PDN they prioritise as soon as possible, will be discussed in detail in section 7.7.

### *7.1.2 Research implications*

Robust measures of sleep should be used in any future research, preferably that have been validated for use with neuropathic pain, for example the MOS scale (Dworkin *et al.*, 2005). It is difficult to use self-report measures for sleep, as these must be completed retrospectively and inherent error exists trying to quantify an experience during which respondents were unconscious. The alternative option, using sleep laboratories, would be costlier but provide empirical measures of sleep duration and sleep architecture (Nicholson and Verma, 2004).

The PROSPERO database maintains a register of completed and on-going systematic reviews. There were studies identified as underway on CBT for primary insomnia and in FMS. There were no systematic reviews investigating ACT for insomnia currently registered (searched December 2016). The UK Clinical Trials Gateway had no studies of psychological interventions for insomnia currently registered (searched Feb 2017).

*7.2 I worry about keeping my physical fitness due to PDN*

In the patient interviews, there was a range of patient discourse about exercise for health. Some participants were acutely aware of altered capacity for exercise and the implications for health, while others did not raise this topic. Although there are technical differences in the definition of physical activity (day-to-day functional activity) and physical exercise (specific activity for health benefits) (Caspersen, Powell and Christenson, 1985), interview participants did not explicitly make this distinction. The following sections will make a distinction where possible, but the researcher is mindful there are significant practical overlaps between these categories.

Physical activity is an important aspect of pain and symptom management for a range of clinical presentations including LBP (NICE, 2009, 2016), FMS (Karjalainen *et al.*, 2009; Busch *et al.*, 2013), osteoarthritis (NICE, 2015a) and fatigue (Cramp and Byron-Daniel, 2012). Promoting physical activity and exercise is central to all musculoskeletal PMPs (BPS, 2013). A recent Cochrane overview (Geneen *et al.*, 2017) included 21 systematic reviews investigating exercise interventions for persistent pain problems; measures of physical function were extracted from these as secondary outcomes. Fourteen reviews (n=129 studies, >9559 participants) demonstrated statistical improvements in physical function, for at least one follow-up time point. Highlighting the results of Busch *et al.* (2007) who reviewed exercise for FMS, as a condition most comparable to PDN, they found aerobic exercise (four studies, 253 participants) significantly improved physical function with a moderate effect size, SMD 0.66 (CI 0.41 to 0.92, p<0.0001).

The effect PMPs have on physical disability has been systematically reviewed. Kamper *et al.* (2015) found measures of disability were reduced by SMD 0.23 (CI 0.06 to 0.40) when compared to treatment as usual (six trials, n=722 participants) and by SMD 0.68 (CI 0.16 to 1.19) when compared to physical treatment modalities (10 trials, n=1169 participants). The review authors note that the included studies were of low to moderate quality and had significant statistical heterogeneity ($I^2$ >90%), so results should be viewed with some caution.

Exercise prescription in PMPs is predicated on helping participants find their baseline of exercise, which does not flare pain, and gradually increase that level. A message that pain does not equal injury is often used (BPS, 2013). The clinical fact that patients with neuropathy can have injury to their feet without the protective experience of pain is a key difference and

consideration. Having insensate feet is not a contraindication to weight bearing activity (Colberg and Vinik, 2014; Sacco and Sartor, 2016), but engaging in physical activity requires checking feet as part of regular self-management behaviour, and all clinicians involved with diabetes should ensure people are performing these checks regularly (NICE, 2004, 2015b).

Chapter 2 found engaging in regular physical activity may not alter subjective pain experience in PDN but may retard pain worsening. Improvement in secondary outcome measures suggest possible benefits to other aspects of life such as increased social engagement (Ahn and Song, 2012) and reduced emotional distress (Dixit, Maiya and Shastry, 2014), these outcomes maybe important to people who valued physical fitness and health. Diabetes clinicians expressed concern that people with PDN may damage their feet if encouraged to exercise without appropriate protection behaviours, however pain clinicians were cognizant of the risk and felt there were alternative exercise options available (Chapter 5, section 5.6.2).

### *7.2.1 Considerations required when prescribing activity*

The term *prescribing* is used deliberately to reflect that patients with PDN are uncertain what to do physically, and so seek advice from medical clinicians. The clinicians who give advice on physical activity need to include what to do, when to do the activity and how long for - this is analogous to advice giving for regimes of prescription medication. Clinicians who prescribe medication should also work with patients to ensure the medication benefits outweigh the side effects and the patient is empowered to understand the medication to optimally self-manage. For activity prescription, clinicians need to work with patients to ensure their advice is acceptable and can fit with the patient's life, and that side effects (tissue break down specifically) are minimised or monitored. The patient will then be in a position to self-manage their activity level.

There are many reasons why a person with diabetic neuropathy might develop foot ulceration. These include foreign objects in their footwear, ill-fitting footwear and tissue loading in excess of that which can be tolerated. A recent study investigating peak plantar pressures (PPP) in the foot, compared weight bearing and non-weight bearing exercises to walking on a level surface (Shah and Mueller, 2012). Weight bearing heel raise exercise was found to increase forefoot PPP by 27% compared to level walking, but there was no difference in PPP for all other weight bearing exercises (climbing stairs, sit to stand, toe raises and single leg stand). The researchers also demonstrated that non-weight bearing exercises (stationary bike, balance ball exercise and active plantar/dorsiflexion) were associated with lower PPP (58-83%) compared to both weight bearing exercise and flat walking. This suggests that different forms of physical activity are likely associated with different levels of risk to insensate feet.

Researchers investigating exercise for peripheral neuropathy have recorded and published rates of adverse events. Shah and Mueller (2012) reported no adverse events related to the exercises in their study. Otterman *et al.* (2011) conducted a pre-post study of cardiovascular and strength exercise with twenty-two people who had diabetic peripheral neuropathy (Otterman *et al.*, 2011). Participants and exercise instructors were advised to conduct appropriate foot checks throughout the study period. Of the participants who completed the exercise programme (n=20/22), 50% had a history of foot ulceration. The researchers reported 58 adverse events of which five were foot related. The authors gave no further details about these events.

A further study randomised participants with peripheral neuropathy between non-weight bearing and weight bearing exercise for a twelve week protocol (Mueller *et al.*, 2013). Participants and exercise instructors were advised to conduct appropriate foot checks throughout the study period. Within the study period 13 superficial foot lesions (seven in weight bearing, six in non-weight bearing arms) and four ulcers (one in weight bearing, three in non-weight bearing arms) were recorded. The study authors highlight these were descriptive results, as the study was not powered for adverse events to be considered an outcome measure.

A major risk factor for foot ulceration is previous history of ulceration. The predicted annual incidence rises from 4.5% in the diabetic population with no history of ulceration, to 31.7% in the population with ulceration history (LeMaster *et al.*, 2008). LeMaster *et al.* (2008) randomised 79 participants with diabetic neuropathy to receive balance and strength exercise in the intervention arm, or foot care advice in the control arm. The participants were followed for up to one year. The authors considered the history of ulceration in the participants (42%) and calculated the predicted likely incidence of ulceration within one year to be 15.9%. At study conclusion, the actual ulcer prevalence of 17% was considered clinically similar between study arms, and to the existing epidemiological data. Balance and strength exercise did not appear to increase rates of ulceration.

History of ulceration is also associated with physical activity levels. A prospective study of 100 participants with diabetes, measured daily steps (Armstrong *et al.*, 2004). Participants were followed for a minimum of 25 weeks (mean 37.1 weeks (SD12.3)) or until they developed a foot ulcer. This occurred in eight participants who were significantly less active than the remaining population (809 steps (SD612) vs. 1394 steps (SD868), p=0.03) and had greater variation in activity level in the two weeks prior to ulceration than the participants who did not ulcerate. The Physical Stress Theory (Mueller and Maluf, 2002) suggests tissues adapt depending on the physical load placed on them. Reduced load leads to tissue atrophy and hence reduced capacity to absorb physical load. Excess load may lead to tissue damage and even death. If load can be applied at an optimum magnitude and rate, tissue hypertrophy occurs and tissue resilience is increased. Recent

studies have used this model to suggest patients could be at risk of ulceration with too little activity, as well as too much (LeMaster *et al.*, 2008; Mueller *et al.*, 2013; Shah and Mueller, 2012). They suggest avoidance of weight bearing activity can lead to tissue atrophy and hence an increased risk of ulceration.

Physical activity has been shown to have a generally positive effect on measures of quality of life for people with persistent pain (Geneen *et al.*, 2017), and it may be that physical activity would have a similar effect within PDN. Research using case series design, and only reporting on quality of life outcomes were excluded from the review presented in Chapter 2, but the studies cited above do suggest some benefit to activity. For example, Otterman *et al.* (2011) found participant perceived limitation of function reduced after the activity intervention (mean -1.4 on a 0-10 scale, CI -0.5 to -2.2, p=0.003) and Yoo *et al.* (2015) found improvements in the BPI-PDN walking, work, relationships and sleep interference subscales following the intervention (all $p<0.02$). These studies were of small sample size and were not randomised, so caution needs to be exercised when considering whether the results are clinically relevant.

The studies included in Chapter 2 and presented above, demonstrate inconsistent reporting of adverse events related to physical activity and so uncertainty remains about the parameters (dosage) of activity (% of full weight bearing, intensity of effort, duration of activity, frequency of activity per day/week/month) that represent the optimum ratio between least risk of foot damage and greatest benefit for physical health, mental health and quality of life measures. The clinicians interviewed (Chapter 5), specifically the secondary care podiatrists, were highly concerned that physical activity could lead to foot damage. The inconsistency of reporting foot-related adverse events means the actual risk of various forms of physical activity cannot be stated with any certainty.

### *7.2.2 Clinical implications*

Prescription of exercise is sometimes considered a simple task; it is unlikely to be so in PDN. Clinicians interviewed were keen to stress that people with PDN would have a range of other diabetes-related complications and other comorbidities that would need consideration (Chapter 5). However, even within 'simple' musculoskeletal clinical settings motivational techniques and other psychological approaches can be necessary to engage people in physical exercise. Diabetes clinicians may need to consider using principles of Motivational Interviewing (Rollnick *et al.*, 2005; McGrane *et al.*, 2015) to help patients initiate and then maintain some form of physical exercise. Studies have used cardiovascular exercise, with intensity based on the person's heart rate reserve (see Chapter 5, section 5.6.2), but there are many exercise options for people with insensate feet including controlled full weight bearing exercise – Tai Chi, pilates, yoga or walking; partial weight

bearing exercise – walking in water or recumbent exercise bikes, or non-weight bearing exercise – hydrotherapy or chair based exercise classes.

Clinicians should be cautious promoting significant pain reduction as the expected outcome. The clinical discussion may need to be biased toward improving other aspects of quality of life (Davies *et al.*, 2015). Consideration needs to be taken of the patient resources (time, money, access), their interests and intrinsic motivation to experiment. Initiating an increase in exercise levels must be gradual and accompanied by regular foot checks (Colberg and Vinik, 2014). As was discussed earlier, a constant challenge in sustaining exercise for health reasons is that the benefits of exercise may not be immediately obvious (Chapter 4 section 4.9.3).

*7.2.3 Research implications – exercise for fitness*

Chapter 5 section 5.6.2 highlighted there were differing professional views on the most appropriate form of activity for people with PDN. Studies investigating physical exercise have specified the nature and intensity of the exercise and this is to be encouraged. However not all studies record rates of adverse events related to foot damage, so the exact parameters of exercise to achieve optimum risk/benefit ratio remain unclear. These are critical data to capture because it would inform both patients and clinicians about the risks involved with increasing exercise levels.

From the patient perspective, every person has differing interests and motivation for physical exercise. Outside of elite sports, the effectiveness for any specific exercise being better than another for fitness, is dependent more on the person consistently participating in the form of exercise, be that Tai Chi, swimming or cardiovascular exercise, rather than the form itself. Physical exercise research to date has focussed primarily on the form of exercise, to elucidate the effect on the participant's pain or quality of life; another approach would be to take the lead from the participant's interest in any form of physical activity and develop that activity as a way toward increased fitness.

*7.2.4 Research implications – activity as exercise*

If a person does not have motivation to engage in exercise, they may have more motivation to engage in some physical activity which has different connotations (to them) than exercise. It would be beneficial to understand more about the links between activity and quality of life in PDN, and what factors are relevant for altering activity levels.

PDN has similarities to other neuropathic pain conditions such as MS and research into physical activity and function from other pathologies maybe useful to consider. In MS, pain is caused by autoimmune breakdown of the myelin sheath surrounding spinal cord neurons. Pain related to MS has impacts similar to PDN with decreased physical function, disturbed sleep

(Braley, 2015), associations with depression and anxiety and is difficult to manage with analgesia alone (Harrison *et al.*, 2015a, 2015b).

Qualitative research with people with MS (Harrison *et al.*, 2015a) described two themes relating to how people manage and cope with their pain experience. One theme was a 'Pain reduction' agenda; here patients described 'fighting' the pain they experienced, and being in a 'Catch-22' position of pain leading to deconditioning, and vice versa. The second theme was a 'Managing and accepting pain' agenda, this was typified by being in touch with their body, knowing their limitations and working with pain, in order to manage it.

The same research team conducted a systematic review of empirical studies to understand the psychosocial variables experienced by people with MS that might be modifiable (Harrison *et al.*, 2015b). They found similar associations between psychological constructs and MS-related function that are present in non-specific persistent pain. Pain catastrophizing was associated with greater pain interference and pain acceptance was associated with less pain interference.

Pain catastrophizing has been shown specifically in PDN to be associated with both increased perceived disability ($\beta=0.311$, $p<0.001$) and reduced quality of life ($\beta=0.373$, $p<0.001$) (Geelen *et al.*, 2016). Pain-related catastrophizing appears to consistently have a mediating role in engagement in function and daily activity, in chronic pain generally (de Boer, Struys and Versteegen, 2012) and neuropathic pain specifically (Harrison *et al.*, 2015b; Geelen *et al.*, 2016). It is unknown how similar the profile of pain acceptance is for people with PDN, to people with MS.

It is currently unknown whether there are associations between acceptance of PDN and either patient day-to-day activity or ratings of quality of life. Using quantitative measures of pain acceptance, such as the BPCI-2 (described in section 6.12.4), in addition to the existing functional measures, would contribute to understanding whether promoting pain acceptance had a positive association with function and quality of life. In conjunction with on-going research in other neuropathic pain conditions, this may indicate which cognitive factors are important in relation to patient function and quality of life and, depending on the findings, whether these are best targeted with CBT or ACT based approaches. For example, there is existing evidence from other conditions, that facilitating acceptance using ACT can mediate quality of life (Nicholas and Asghari, 2006), whereas challenging catastrophic thinking can be approached using ACT (Hughes *et al.*, 2017) or CBT (Pincus and McCracken, 2013) approaches.

*7.3 PDN makes walking difficult*

Walking is a human function that spans the dichotomy between activity and exercise (Caspersen, Powell and Christenson, 1985). Walking has a critical function, both in its own right for activity and pleasure, and as a method of moving around the environment to achieve daily

tasks. Interview participants described the difficulty of walking, even short distances, with PDN. Further to this, people with PDN have a higher risk of amputation than those without (odds ratio 1.52 (CI1.15 to 1.99) (Ritzwoller *et al.*, 2009)). The interview sample (n=23) included one person with unilateral amputation and one person with bilateral below knee amputations. People with amputations due to neuropathy would experience additional impediment to walking.

For PDN it would not be clinically appropriate to suggest a person avoid walking completely due to the potential consequences for general health and DM management, or, that they walk with no regard for the amount of pain they experience. Rather, a graded, moderate approach to walking would be appropriate, and in-line with advice for other long term conditions such as FMS (Busch *et al.*, 2013; Karjalainen *et al.*, 2009), chronic obstructive pulmonary disease (Güell *et al.*, 2000) and chronic non-specific pain (Geneen *et al.*, 2017).

Guidance for healthy levels of physical activity have been translated as equivalent to 10,000 steps daily. This guidance has been studied with participants who were obese (n=35) (Castres *et al.*, 2016). Using pedometers to count daily steps over a six-month period, participants were encouraged to increase their daily step count by 1000 per week, until at 10,000 steps daily. At post-intervention, there were changes in body mass (mean -3.8kg, $p<0.01$), hip circumference (mean -4.6cm, $p<0.05$) and anxiety (HADS questionnaire) (mean -1.2, $p<0.05$). However, the validity of 10,000 steps daily is not a complete surrogate marker for achieving the advised time intensity levels (150 minutes/week in 10-minute intervals) of physical activity (White *et al.*, 2013). White *et al.* (2013) provided participants with both pedometers and activity monitors. Activity monitors record time as well as steps, so can establish the consistency and continuity of activity (time intensity) rather than just a sum total of steps for the day. The study found only moderate positive predictive value, that participants with a step count ≥10,000 steps/day were meeting the time intensity guidelines (Men: sensitivity 46.5, specificity 85.2, positive predictive value 16.7; women: 67.9, 90.3, 26.7 respectively) (White *et al.*, 2013). For health benefits to accrue walking must be at an appropriate intensity and volume and strategies to both motivate and facilitate people to achieve these variables are critical.

### *7.3.1 Clinical implications*

As stated above, walking is critical for daily function and restrictions have potential further impacts on physical and mental health. There appear to be a number of causes for reduced walking. These include the severity of pain experienced (Hoffman *et al.*, 2010), but also the degree of worry and fear related to physical function (Geelen *et al.*, 2016; Selvarajah *et al.*, 2014).

Techniques to facilitate walking may include provision of walking aids such as elbow crutches. Crutches have been shown to reduce the foot PPP in people with diabetic neuropathy

and to increase the sense of balance and security (Kwon and Mueller, 2001). This potential benefit needs to be considered against the obvious impediment to upper limb use. Since PDN is not causally related to weight-bearing it is not clear whether use of crutches would necessarily reduce the impact of PDN on walking.

The use of activity monitors and setting specific goals may help to motivate people to gradually increase their walking capacity. Overlap exists here with the previous section since appropriate foot checks are required as part of self-management. It is appropriate to suggest that clinicians involved with PDN need to have practical skills to help people engage in some physical activity with due regard for foot protection and existing comorbidities. These practical skills include effective communication to facilitate exploration of the thoughts and beliefs the person has about physical activity.

In addition to practical physical approaches, clinicians need to help patients consider their own cognitions regarding walking. People who have struggled with walking for years may well develop a range of discouraging or hopeless thoughts and beliefs. The process of slowing down the cognitive process to understand thoughts better is a fundamental approach of CBT (Vlaeyen and Morley, 2015). CBT aims to help patients consider the validity of their cognitions and when necessary whether they can be reappraised to be less negative. In contrast, rather than reappraising thoughts, ACT aims to help people disengage from negative thoughts, or to reduce their reactions to these thoughts (McCracken and Vowles, 2014). Currently there are PMPs based on CBT and ACT approaches. Helping patients to deal with negative cognitions are central to these programmes, whatever the philosophical underpinnings. Not enough is currently known about the cognitions that are prevalent for people with PDN, to suggest whether CBT or ACT represents the most appropriate clinical approach.

Walking was a specific function that emerged as a code from the patient interviews and consequently was presented in the Internet survey. The twin approaches of 1) a paced graded physical approach to the activity combined with 2) considering what cognitions are associated with an activity, and then challenging or managing these where necessary, could be applied to any functional activities of importance to the person.

### *7.3.2 Research implications*

It is important that robust measures of walking function are used in future research. There are numerous measures of physical function; the Walk-12 test was originally developed to measure walking function in MS but has been validated for peripheral neuropathy generally (Graham and Hughes, 2006). In much the same way that Section 7.2 focussed on loss of physical fitness and how clinicians may encourage patients to engage in a variety of physical activities in a

manner that would not increase their risk of foot damage or potential amputation, research into walking requires individualised protocols to establish the person's baseline walking and measure their daily step count (Castres *et al.*, 2016). This graded approach will help to elucidate the appropriate dosage of walking. This may be achieved and facilitated using a pedometer or smart phone activity monitor (Smith *et al.*, 2004). Future research on walking needs to evaluate the changes to measures of walking using measures such as the Walk-12, but also explore the associations with patient's quality of life, rather than pain severity alone.

*7.4 PDN causes me to have numb feet*

Diabetic sensory neuropathy, without pain, is the most common form of peripheral neuropathy (Waldman, 2000). Loss of afferent cutaneous sensation reduces the normal response to tissue damage, which then predisposes to tissue ulceration. Sensory loss affects afferent proprioceptive information relating to joint position sense; this information is critical for balance and locomotor control (Peltier, Goutman and Callaghan, 2014).

There is evidence from basic science that physical movement can affect the nerve physiology that underpins sensory neuropathy. Axoplasmic fluid acts as the transportation medium in neurones, carrying ion channels from the cell body to their destination in the cell membrane, and intracellular signalling molecules back to the cell body. This fluid becomes more viscous when neurones are held static, and less viscous when moved, a thixotropic property (Bove, 2008; Dilley and Bove, 2008). This physiological property underpins neurodynamics, an aspect of manual therapy and active exercise common in physiotherapy (Nee and Butler, 2006).

Research has found positive correlations between neurodynamic test responses and responses to manual palpation of nerve tracts, although the participant groups experienced musculoskeletal neuropathic pain, rather than related to diabetes (Walsh and Hall, 2009; Schmid *et al.*, 2009). Kumar *et al.* (2011) assessed patient responses to straight leg raise and manual palpation of neural tracts in the lower leg in healthy participants, and people with diabetes, sensory neuropathy and PDN. The group with PDN had straight leg raise range of mean 41.2˚ (SD15.8) and were sensitive to palpation of their peroneal and tibial nerve tracts. The non-diabetic control group had straight leg raise range of 81.8(SD4.8)˚ and experienced no symptom provocation on palpation (Kumar *et al.*, 2011). These results suggest these clinical assessment techniques have validity for diagnosing the presence of neuropathy symptoms and so consequently may have use in treatment.

There have been attempts to explore neurodynamic treatment for PDN. Neurodynamic treatment involves specific sequences of body movements to increase the mechanical load in a nerve tract at one end, whilst simultaneously off-loading the tract at the other end. The

participant's tibial nerve may be caused to 'slide' longitudinally by combining hip flexion with ankle plantar flexion, then moving to a position of hip neutral with ankle dorsiflexion. There is strong evidence such combinations of movements differentially move neural tissue compared to surrounding structures (Coppieters and Butler, 2008; Coppieters *et al.*, 2006; Coppieters, Hough and Dilley, 2009; Alshami, Souvlis and Coppieters, 2008). Differential sliding of neural tissue is thought to be beneficial to axoplasmic viscosity and intra-neural metabolic processes thus may have a direct effect on the pathophysiology leading to sensory neuropathy.

A treatment intervention for PDN, of physical movements to 'slide' the sciatic, peroneal and tibial nerve tracts was compared to passive movements of the contralateral ankle and foot joint structures for the same treatment duration (Kumar *et al.*, 2010). Eligible participants (n=44) were randomised to receive the neurodynamic intervention to either their left or right leg first, followed by the sham intervention to the opposite leg. The study recorded vibration, and hot and cold perception thresholds. On the side treated using neurodynamic exercise, there were improvements in all the outcomes measured. The changes suggested improvements in sensory physiology of the nerve tracts. However, the post-treatment follow up was limited to 15 minutes, so whether changes were sustained or clinically meaningful is unknown.

The same research group conducted a small-scale randomised study (n=32) using neurodynamic exercise for the common peroneal nerve, in addition to a standard package of care (walking prescription, diet and lifestyle changes) (Kumar, Adhikari and Jeganathan, 2012). This study had a five-week follow-up period. The addition of peroneal nerve exercises improved vibration perception and thermal perception thresholds, as well as measures of pain and quality of life. The study has only been reported as an abstract which did not present participant co-morbidities or other data needed for full appraisal.

The study by Kluding *et al.* (2012) has been described earlier in section 7.2. In addition to the outcome measures described, skin biopsy was used to visualise intra-epidermal nerve density and axonal branching. A reduction in nerve fibre branching is a hallmark of small-fibre neuropathies such as PDN. There was an increased density of branch nodes per nerve fibre after exercise intervention, from mean 0.16(SD0.15) to 0.27(SD0.19) ($p=0.008$) at the proximal biopsy site (20cm from iliac spine, lateral thigh) but not in the distal biopsy site (10cm above lateral malleolus). There were no changes in nerve conduction or quantitative sensory testing. The authors highlight the changes in density seen at the proximal site, but not the distal site, may reflect the greater severity of distal pathophysiological changes (Kluding *et al.*, 2012).

Numb feet are often associated with increased risk of falling (van Schie, 2008). A systematic review found six eligible studies examining interventions to improve balance in peripheral

neuropathy (Ites *et al.*, 2011). Only one study investigating lower limb strengthening exercises (wall slides, single leg stands, open and closed chain ankle strengthening) was found to improve measures of balance (Richardson, Sandman and Vela, 2001). This single-blind controlled study was small scale (20 participants randomised to each arm) but all participants had diabetes-related peripheral neuropathy. Measures of balance (tandem stance, functional reach and uni-pedal stance) all improved in the intervention arm compared to the control arm ($p<0.004$ at post-intervention time point).

### *7.4.1 Clinical implications*

There have been small scale studies exploring the role exercise may play in improving nerve function, but the evidence is currently limited. Strength and balance exercises may help to maintain proprioceptive responses and so reduce the risk of falls (Richardson, Sandman and Vela, 2001). Movement of any kind – neurodynamics (Kumar, Adhikari and Prabhu, 2011), Tai Chi (Hung *et al.*, 2009) and cardiovascular exercise (Kluding *et al.*, 2012) – may alter the pathophysiological changes that occur in neural tissue and lead to sensory neuropathy, but further research is needed.

The key clinical management for numbness is prevention through glycaemic control (Peltier, Goutman and Callaghan, 2014; Smith *et al.*, 2006). There are no current pharmacological options for treating the sensory loss (Prof Wynick, personal communication), this maybe because numbness is inherently less distressing than the painful aspect of PDN and so does not merit pharmacological research focus.

Patients may have to accept that numb feet are an aspect of PDN that cannot currently be treated.

### *7.4.2 Research implications*

Research participants have often had diabetes and PDN symptoms for many years. Duration of diabetes and relatively poor control of blood sugars are the key causes for development of sensory neuropathy and PDN (Peltier, Goutman and Callaghan, 2014). A Cochrane review has highlighted that increasing exercise and making dietary changes in the pre-diabetic stage can reduce the relative risk of developing diabetes by 37% (Orozco *et al.*, 2008). Early intervention to prevent the onset of diabetes is more successful than dealing with the consequences. Studies investigating exercise, whether for possible improvements in pain, numbness or balance, need to recruit people earlier in their journey with PDN. Since the pathophysiological changes of PDN appear irreversible, it seems intuitively sensible to research the potential for non-pharmacological strategies earlier in the process of pathological development, with the aim of preventing significant impacts, such as disability and distress.

Randomised controlled studies need to be conducted that investigate whether intervention with specific exercises such as yoga (Willis Boslego *et al.*, 2017), neurodynamics (Kumar, Adhikari and Prabhu, 2011), Tai Chi (Ahn and Song, 2012) and/or cardiovascular exercise (Dixit, Maiya and Shastry, 2014; Toth *et al.*, 2014) can arrest the development of sensory neuropathy and potentially PDN. It would be critical that these studies have sufficiently long follow up duration to help inform the question of PDN prognosis, and that they record and report on foot-related adverse events to help establish the appropriate dosage of exercise. This research recommendation is relevant to all the impacts prioritized by survey respondents.

There are however organisational difficulties in recruiting people to research earlier in their journey with PDN. Chapter 1, section 1.1.4 highlighted that pre-screening to predict the later development of DM is limited by moderate specificity and sensitivity of HbA1c (Barry *et al.*, 2017). Once diagnosed with DM a patient should receive annual health checks including nerve function assessment as recommended best practice by NICE and QOF guidance (NHS Employers, 2016; NICE, 2004, 2015b). However, the primary care practice nurse, a clinician who conducts annual diabetes checks, highlighted the computer system proforma did not have the capacity for identifying pain complaints other than as 'free-text'. Similarly an audit of pain clinic activity (BPS, 2012) found neuropathic pain appeared under-represented in the clinical coding structure used (Read Codes). These information technology issues currently make it more difficult for researchers to find and alert people with symptoms of PDN to active research studies.

*7.5 I am worried that PDN will get worse in the future*

Interview study participants were concerned about their prognosis with PDN; this was not helped by the frequent failure of medications to adequately control their symptoms, and lack of information regarding strategies beyond medication management. The natural history of PDN is not however certain (Peltier, Goutman and Callaghan, 2014). Chapter 6, section 6.12.1.2 detailed the few studies which have followed people with PDN over time. Clinicians are unable to confidently alleviate peoples' fears that PDN will get worse resulting in a degree of patient uncertainty. The survey questions (Chapter 6) were specific to PDN, but it is possible the respondents' worries for the future included other facets of diabetes and other health conditions.

More broadly, the interview study theme "A range of negative emotions", included codes identifying specific worries about fitness and future financial security, and the future in more general terms. Worry, conceptualised as negative fears for the future, is the cognitive hallmark of catastrophization and there exists a large body of research exploring such cognitions in people with pain (Sullivan, Lynch and Clark, 2005; Vowles, McCracken and Eccleston, 2008; van Damme, Crombez and Eccleston, 2004). Higher levels of catastrophizing have been associated with greater pain severity (de Boer, Struys and Versteegen, 2012), and lower physical activity levels, mental

health and overall quality of life (Osborne *et al.*, 2007). For these reasons, aiming to reduce catastrophic thinking is a common psychological aim for PMP based within CBT (Smeets *et al.*, 2006) and ACT principals (McCracken, Gauntlett-Gilbert and Vowles, 2007).

### *7.5.1 Clinical implications*

The similarity between PDN and MS-related pain has been discussed in this chapter (section 7.2). People with MS have a similar uncertainty of how life with their condition may progress over time. Chapter 6 has previously discussed the difference between active coping strategies and acceptance strategies (Chapter 6, section 6.12.4). People with PDN may find it helpful if clinicians considered a range of approaches beyond medication. Firstly, medication strategies need to be optimised, with a clear message to patients that they are not curative. Medication is unlikely to completely eradicate the pain but can be an aid to function.

Secondly, clinicians need to self-evaluate the style and manner of their clinical communication to ensure they give the patient the full freedom to raise the issues most important to them. Clinicians may need to develop skills in asking open, non-judgmental questions, these questions give the person the opportunity to raise issues which they may not associate as being part of the clinician's role. Physiotherapists, for example, have been encouraged to develop skills to inquire about mood state (Main *et al.*, 2012), an aspect of life that patients may not associate with physical therapy (Cooper, Smith and Hancock, 2009).

Thirdly, in many chronic health conditions with a range of potential futures, worry will be an additional burden on the patient, and unlikely to be beneficial or lead to improvement in their quality of life (Eccleston and Crombez, 2007). Addressing worry has likely therapeutic benefits irrespective of the cause.

Lastly, clinicians need to consider whether they have the necessary range of strategies to help people address and manage the most important impacts of PDN. If the clinician does not have the strategy/ies required, they need referral routes to clinical colleagues who maybe better equipped to help the person.

This suggested approach aims to help the clinician understand the issues the patient is most worried about. Depending on the issues, there may be appropriate clinical strategies to reduce worry and catastrophizing. Where such strategies are not available the clinical focus maybe toward helping people to accept their pain experience, develop resilience to pain and despite its presence, engage with life.

*7.5.2 Research implications*

In order to reduce the impact of being worried that PDN will get worse in the future, more needs to be understood about its natural history. Such longitudinal research would be facilitated by a consistency of clinical coding used on primary and secondary care IT systems. This would allow data searches looking for correlation of codes related to DM and neuropathic pain, or preferably a specific code for PDN, and the initiation and cessation of the range of medications recommended for PDN. Presence of conditions that might require prescriptions of the same neuropathic pain medication (nerve root pain) would need to be retrieved and excluded. The current system of Read codes is being retired by April 2018 and replaced with SNOMED CT codes. Whether the new coding system will allow specific codes for PDN is unknown.

More research is needed to better understand coping strategies and quality of life in people with PDN. The survey in Chapter 6 used the CSQ, this assesses coping on two scales of active and passive coping strategies. It may have been more relevant to use outcomes such as the BPCI-2 or Chronic Pain Acceptance Questionnaire. These questionnaires could be used in longitudinal cohort studies to investigate whether different approaches to coping and traditional active strategies were associated with changes in function and patient quality of life.

*7.6 PDN leads me to feel depressed*

Depression has been defined as "a negative schemata about self, the future and the world, which when activated by stressful life events results in processing bias that distorts perception and maintains the negative thought pattern, and with them the mood itself" (Pincus and Williams, 1999). From the patient interview study, it was clear there were many sources of stress for people with PDN that may have contributed to the experience of depression – pain, work, finances, daily restrictions, interrupted sleep and altered relationships. These issues are not uncommon with persistent pain states of any cause.

Depression in PDN is complex, with the experienced mood a potentially unique combination of 'depression associated with diabetes' (Chapter 1, section 1.1.6), 'depression associated with persistent pain' (Chapter 1, section 1.2.4.2) and 'reactive depression associated with daily restrictions to personal agency and independence' (Pincus and Williams, 1999). The presence and contribution of each of these factors will be different for each person. The presence of depression (of any cause) has close links with reduced self-management behaviours and social interaction, increased sedentary behaviours and rumination – cognitive and behavioural variables that tend to worsen both pain experience (Gatchel *et al.*, 2007, 2014) and diabetes management (Petrak *et al.*, 2015).

*7.6.1 Clinical implications*

Clinicians need to open conversations with patients about their mood and the impact that has on consequent pain, behaviours and overall quality of life. Where necessary, they then need a range of clinical options to help the patient.

Of the range of advised medications for PDN, Duloxetine has a centrally acting, anti-depressant effect. Duloxetine appeared to have greater benefit in reducing pain, pain-related interference and improving mood states, than peripherally acting anti-epileptic medications (Pregabalin and Gabapentin) (Happich *et al.*, 2014). These findings, however, were based upon a review of clinical practice, rather than a controlled randomised trial.

Physiotherapists manage depression by helping people to set goals to achieve a measure of success and hence reduce the negative perceptions held (Main *et al.*, 2012; Carnes *et al.*, 2013). These goals must be of importance to the person and specific, realistic and time-limited. Achieving the goal is likely to increase the person's confidence to set and achieve further goals with increasing independence, resulting in reduced depression. This clinical approach is widely used for inflammatory (Dures *et al.*, 2012) and non-inflammatory arthritic pain (NICE, 2015a).

PMPs for persistent pain have a variety of psychological approaches for managing depression. CBT-based programmes help participants to identify cognitions and then evaluate the accuracy and validity of those cognitions. Unhelpful cognitions may then be challenged and potentially reappraised (Morley and Williams, 2015; Vlaeyen and Morley, 2015). A Cochrane review of psychological therapies for pain extracted mood data as secondary outcomes. CBT compared to treatment as usual, had a positive effect on mood at the post-treatment time point, with SMD -0.38 (CI -0.57 to -0.18, 12 studies, n=899 participants). This effect was reduced at follow-up to SMD -0.26 (CI -0.51 to 0.00, 7 studies, 637 participants) (Williams, Eccleston and Morley, 2012).

ACT-based programmes help people to gain distance from their cognitions hence reducing unhelpful responses to those cognitions (Morley and Williams, 2015; Vlaeyen and Morley, 2015). A systematic review of ACT for persistent pain extracted measures of depression as secondary outcome data (Hughes *et al.*, 2017). The ACT interventions resulted in significantly better levels of depression immediately post treatment in comparison to control, with a SMD -0.52 (CI -0.80 to -0.24). This effect was reduced at three-month follow up (SMD -0.52 (CI -0.90 to -0.14)) and became insignificant at six-month follow up (SMD -0.85 (CI -1.90 to 0.13). The analysis at 3-month time point had large heterogeneity ($I^2$ 80.5%). Once an outlying study was removed $I^2$ was reduced to 0% and the effect size quoted above was calculated. This outlying study was however

included in the analysis of the six-month follow-up data and may explain the wide 95% confidence intervals.

The review by Hughes at al. (2017) included one study that compared ACT to CBT (Wetherell *et al.*, 2011). This study (n=114 participants, age range 18-89 years, mean age 54.9 years, 30% neuropathic pain) assigned consecutive patients to treatment groups. The groups were then randomised to either receive ACT or CBT-based intervention. There were changes in Beck Depression Inventory scores for ACT arms (n=57) (mean change -2.32(SD5.87), p=0.004) and CBT arms (n=57) (mean change -3.18(SD6.45), p=0.0005) at post-treatment. At six-month follow up changes in depression had become non-significant for both arms. Hughes *et al.* (2017) calculate the data favoured CBT over ACT with a small effect size of SMD 0.39 (CI 0.02 to 0.76) at the post-treatment time point; this became an insignificant effect at later time points.

Specific to the impact of depression, there are data to support both CBT and ACT approaches. Both psychological approaches have support for the cognitive impacts identified by the survey, which were: worry about fitness, the future, and depression. The lack of clarity between psychological approaches appears consistent with the wider research into psychological therapy in pain, where strategies to select the appropriate approach for the person, rather than the appropriate approach for the impact, is suggested as a future direction of research (Vlaeyen and Morley, 2015). If medical/psychological interventions are to be person-centred then understanding which approach is likely suited to each patient is important.

### *7.6.2 Research implications*

The correlation analysis presented in Chapter 6 found strong associations between passive approaches to coping with PDN and the severity of the impacts. Trying to avoid the pain or hoping it would not flare did not ameliorate the experience of PDN. However, using active coping approaches, at least as defined by the CSQ, were not associated with any lessening of impact.

If unpredictable pain flares are interfering with achievement of day-to-day activity and contributing to a person's depression, novel strategies to manage unpredictability need to be considered. Strategies of activity scheduling and pacing place the management strategy before the activity; it maybe the activity needs to be foremost, and strategies to manage a pain flare used when and if that flare occurs. Such strategies might include focus on the present moment, rather than possible futures, as advocated by ACT and MBSR.

The hypothesis that acceptance-based approaches are associated with reduced distress and improved quality of life could be studied using either a controlled design or a case-series design. Were a controlled design used, care would be needed designing the control intervention. Moore *et al.* (2010) highlighted that control interventions must have the same credibility as the active

arms, so non-psychologically directed treatment-as-usual would not be an appropriate comparison. Here a case series design, with a waiting list control time period, maybe appropriate. The hypothesis would be that a positive relationship would be found between changes in pain related acceptance (using the BPCI-2) and changes in measures of function and/or distress at post-intervention.

*7.7 Is there a need for a multidisciplinary Impact Coping Skills programme for PDN?*

For some people with PDN, who are distressed and disabled, a multidisciplinary approach seems warranted. For other people, it seems appropriate to suggest that individual clinicians in primary and secondary care could develop a range of skills to help the individual patient with the specific issues they raise.

The dispersal of skills, particularly in psychological management, from specialist teams to individual clinicians has occurred in the management of LBP. Multidisciplinary PMPs including psychological management, were restricted for the most distressed patients due to limited capacity (Phillips *et al.*, 2008). Developments in stratifying LBP by risk factors identified as prognostic for the development of persistent pain, highlight that people may require psychological support in the early stages of LBP, not just once pain has been present for a significant time (Foster, Hill and Hay, 2011; Hill *et al.*, 2011). These developments have required clinicians other than psychologists, particularly physiotherapists, to develop skills in identifying and managing psychological aspects of fear, worry and stress (Main *et al.*, 2012).

Some clinicians interviewed identified a discrepancy of skill mix between paediatric MDT teams, which would nearly always have access to clinical psychologists, and adult MDT. Patients in adult secondary care services were more likely to have developed complications but would have much less access to psychologists (Chapter 5, section 5.5.2.5). Up-skilling the range of clinicians involved in DM and PDN, to effectively address psychological issues would help to alleviate this issue.

The term PMP is used within this thesis to define a multidisciplinary intervention that aims to help participants live with pain. This term is common in research literature and clinical practice and the connotation understood both nationally and internationally. The term may imply to patients however, that their pain is the focus of management, whereas reduction of subjective pain is rarely the stated aim of these programmes. Rather, the focus is on quality of life with pain. A more appropriate term than PMP maybe “Impact Coping Skills Programme”, it would be important to explore this and other alternative terms using focus groups with both patients and clinicians to establish the most acceptable descriptive label.

The components described in sections 7.1 to 7.6, could be delivered by individual clinicians, either in primary or secondary care, or as part of an MDT programme with a focus on PDN. This makes future studies into improved management for the impacts of PDN prioritised by respondents in Chapter 6, challenging. A tension exists between creating management packages individualised to a patient's priorities and delivering a package of strategies in a group format, that aims to cater for the most frequently identified priorities but is bespoke to no-one. Chapter 6, Table 29 outlines how the top-6 priorities presented in this chapter, had some consistency (for example sleep) but were not universal to all sub-groups.

If a patient-centred approach were taken, the study design would need to be a case series with patients acting as their own control. Appropriate outcome measures for the specific impact of PDN would be taken at baseline ($time_0$), pre-intervention ($time_1$), post-intervention ($time_2$) and longer term follow up ($time_3$). Although aligned with clinical practice this study design lacks randomisation, consistency of outcome measures, blinding of researchers to treatment allocation and suffers from an inconsistency of intervention delivery.

An alternative would be to design the curriculum for a PDN Impact coping skills programme and perform a pilot study. Patients could be randomised between intervention and control arms, a battery of outcome measures could be consistently recorded, the intervention manualised for consistency and delivered by clinicians not involved with the data collection. There are three options for randomisation: 1) randomise eligible, consenting individuals from recruitment sites to intervention or control arm; 2) select recruitment sites with similar referral rates, social and demographic variables and run the intervention in one site, comparing data to the control site. This option cannot guarantee that the arms will be equitable at baseline and there may be unconsidered factors present in the sites that bias the data. And 3) to randomise the delivery of an Impact Coping Skills Programme between study sites, but delivered by the same clinicians for consistency.

It is clear future research designs should consider potential MDT Impact Coping Skills Programme as 'complex' interventions as defined by the Medical Research Council (Walach *et al.*, 2006; Craig *et al.*, 2008). Such an intervention fits the criteria for complex because there are multi-directional interactions between the person's physical state and psychological state (depression, anxiety, stress and motivation to name four). There are further interactions with the person's social situation - how much support people have from family, peers, Internet social media groups, primary and secondary care medical teams. Lastly, the person is likely to have additional diabetes-related complications (see Chapter 1 section 1.1.8) and potentially other medical conditions which they have to manage. Recent studies have used the Medical Research

Council framework to guide the development of pain self-management courses for general musculoskeletal pain (Carnes *et al.*, 2013).

*This chapter has described the top six impacts that respondents with PDN identified as their priorities to have better strategies to manage. For some impacts – sleep disturbance, physical fitness, functional walking, worry and depression – there are existing strategies in PMPs that could be applicable to the population with PDN. Clinicians advising physical activity will need to be appropriately aware and cautious of the need for foot protection and checks. They will also need to take other potential co-morbidities into consideration. In PMPs the impacts on mood have been addressed using both CBT and ACT approaches and further research is required to understand whether one approach would be more beneficial in PDN than the other. There is much less evidence regarding interventions for the impact of numb feet.*

*The management strategies outlined above could be delivered according to individual patient need, or brought together to form a PDN Impact Coping skills course. The on-going physiological processes of DM suggest that moving interventions 'up-stream' would be beneficial rather than waiting for the impacts to become established.*

*The following chapter will summarise the thesis including strengths and limitations as well as some personal reflections.*

# Chapter 8 – Thesis summary

*The previous chapter examined the top priorities selected by survey respondents and considered the clinical and research implications of each. This chapter will summarize the overall thesis findings, considering the strengths and limitations of each, and highlight the new knowledge that this thesis contributes to the field. It will also provide a personal reflection.*

## *8.1 Thesis summary*

The aims of this thesis were set out in Chapter 1, section 1.6.2 and are considered in the following sections.

*Aim 1) To conduct a systematic literature review of the evidence investigating physical activity and psychological coping strategies, in the management of PDN.*

Chapter 2 detailed a systematic review of the literature that retrieved studies investigating physical activity or psychological coping strategies for PDN. Measures of pain severity were specified as primary outcome data and other measures of quality of life were considered secondary outcomes. Few studies were found. Two studies investigating physical exercise found inconsistent results. Aerobic exercise did not improve pain rating, the statistically significant results presented were due to the control arm worsening (Dixit, Maiya and Shastry, 2014). Tai Chi did improve pain severity but the study was not powered for pain as an outcome measure and the control arm worsening contributed to the statistical significance (Ahn and Song, 2012).

The above physical activity studies did show a positive effect of physical activity on measures of quality of life for participants in the intervention arms. However, quality of life was not the primary outcome of interest in this literature review, and so all available studies were not systematically retrieved. These findings for physical activity were broadly in-line with the recent Cochrane overview for chronic pain (Geneen *et al.* (2017), where activity was shown to have more consistent positive effect on function and quality of life, than pain severity.

Two studies investigating psychological approaches were also included: CBT (Otis *et al.*, 2013) and mindfulness relaxation (Teixeira, 2010). Otis et al. (2013) was biased by a small sample size and high attrition rate, and Teixeira (2010) did not have adequate blinding of researchers. Chapter 2 found there was currently insufficient evidence to conclude whether psychological therapy had a role in the management of PDN.

*New knowledge*

- There is limited evidence for pain management strategies in managing PDN specifically.

*Future research considerations*

- Future research should consider strategies to manage quality of life more broadly, than focus on pain severity in isolation.
- Patient and clinician opinions of PMP strategies are unknown therefore two interview studies were designed to explore these.

*Aim 2) To explore peoples' experiences of living with and self-managing PDN, and their perspectives on physical activity and psychological coping strategies for PDN management.*

An interview study was conducted with people who experience PDN. The methodology was described in Chapter 3 and the results presented in Chapter 4. This study found PDN had a wide range of impacts on peoples' lives. These impacts were more varied than had been captured previously by research using quantitative questionnaires (Alleman *et al.*, 2015). Participants' experiences of medical management were usually based on medication, with no adjunctive strategies suggested. They had experimented with a variety of management strategies themselves, usually to no benefit. There was scepticism about how physical activity or psychological approaches could be beneficial for PDN, but those who had attended PMPs for other reasons felt the strategies did have applicability to PDN.

A strength of this study was the consistency of research approach from research questions formulation to data collection and analysis. Using one-to-one interviews allowed participants to freely discuss their experiences and management of PDN. Careful supervision and guidance from the supervisory team helped to ensure the data and analysis were not prejudiced or biased by the novice researcher. The repeat coding and analytic approach (described in Chapter 3, sections 3.11.4 and 5) ensured the participants' views were accurately reflected in the results and conclusions.

There were two key limitations. Firstly, the lack of ethnic diversity (22/23 participants identified as White British). Pain has many cultural and social nuances (Edwards, Fillingim and Keefe, 2001) and while qualitative research does not claim to be generalizable beyond the sample population (Petty, Thomson and Stew, 2012a), it was disappointing not to recruit a sample with wider ethnic diversity. Later studies (Internet survey, Chapter 6) were developed based on the

codes identifying the impacts of PDN generated by this interview study. These codes were developed from an ethnically homogenous sample and this limitation needs to be recognized for its influence on the later study.

Secondly, most interview participants had not attended PMPs so their perspectives were not based on experience. The participants who had attended PMPs for other pain experiences felt the strategies could be applied to PDN.

*New knowledge:*

- The impacts of PDN are broader and more varied than reflected by published studies based on existing questionnaires.
- Physical activity, for some people with PDN, acts as a distraction, or they alter their expectations for a specific activity in order to maintain general activity levels.
- In relation to psychological support, those who have experienced contact with psychologists, either through PMPs or individual psychology appointments, find this beneficial for considering and challenging negative cognitions.
- Views on how applicable physical activity and psychological support are individual to the person and cannot be generalised to the pathology of PDN. Some patients would be more open to a PMP approach than others.

*Future research considerations*

- To explore the treatment priorities of patients further, an Internet survey was designed using the impacts developed in the patient interview study.

*Aim 3) To explore specialist clinicians' current strategies for management of PDN (as one form of diabetic complication), and their perspectives on physical activity and psychological coping strategies for PDN management.*

An interview study was conducted with specialist diabetes clinicians, specialist pain clinicians and representatives from primary care who had experience of treating people with PDN. The methodology was presented in Chapter 3 and the results in Chapter 5. It was clear from the diabetes clinicians they were aware of the range of impacts experienced by people with PDN, specifically highlighting sleep disturbance, depression, anxiety, mobility issues and social isolation. Yet they described having few strategies beyond medication to manage these impacts. Diabetes clinicians raised two specific concerns regarding strategies from PMPs, 1) that people with PDN were at risk of tissue damage if excessive physical activity was advised and 2) that people with DM

and PDN would likely have a range of other complications and comorbidities that made them medically more complex than the 'usual' participants in a PMP.

Pain specialist clinicians described many PMP strategies could be applicable to people with PDN. They were aware some strategies, particularly pacing physical function, may not be so applicable and novel strategies maybe required. This finding was supported by other research, for instance Daniel *et al.* (2015), who described difficulty accommodating the specific needs of people with neuropathic pain in 'standard' PMPs. Pain clinicians were cognisant of the risks physical activity could pose to insensate feet but had other non- or partial-weight bearing exercise options available to minimise that risk.

By using one to one interview the clinicians interviewed were able to give their opinions freely. Because interviews were conducted over a number of months, issues raised in one interview could be explored further in subsequent interviews if necessary. There were limitations to the sample population. Only secondary care podiatrists were interviewed, so the perspectives of primary care podiatrists, whose role is ulcer prevention rather than treatment, may differ. Only one GP and one practice nurse were recruited and so there may have been other primary care experiences of managing PDN that have not been captured.

*New knowledge:*

- Diabetes clinicians are aware of the wide-ranging impact of PDN but only routinely consider medication.
- Diabetes specialists and primary care clinicians considered all PMP strategies were potentially beneficial to people with PDN, but with two caveats: people with DM were likely to be more medically complex than those with MSK pain conditions, and there were risks of foot damage associated with physical activity.
- The perspectives of diabetes clinicians were not based on direct experience of PMPs.
- Pain specialist clinicians have options to adapt physical activity to be suitable for people with PDN.

*Future research directions*

- The concerns of diabetes clinicians will be vital to consider and address in future research.

*Aim 4) To explore which impacts of PDN people prioritise for improved, or alternative, management strategies.*

Based on the impacts described in Chapter 4 (Aim 2), an Internet survey was created to explore how frequent and severe these impacts were, and to establish respondents' priorities for improved management strategies (Chapter 6). In essence this study aimed to build management strategies based on the patients' experiences and priorities, rather than by clinicians assuming what strategies were required by their patients. Of the 58 impact statements, only four were experienced by less than half of the survey respondents. This highlighted how extensive, and varied between individuals, the impact of PDN can be on peoples' lives. This finding provided an element of triangulation to the impact results of the interviews (Mays and Pope, 2000; Doyle, Brady and Byrne, 2009). These impacts reduced patients' quality of life, and this was in-line with existing research (for a summary please see Alleman *et al.* (2015)), but critically, these impacts included issues not present in the usual questionnaires used in PDN quantitative research. The body of research using these questionnaires as outcome measures, may not be measuring outcomes of relevance to the population with PDN.

The study explored associations between the impacts experienced, and active or passive pain coping strategies. There was strong positive correlation between passive coping (as defined by the CSQ) and worsening impact of PDN, but active coping was not correlated with less impact. The constituent factors of active coping were congruent with the management strategies of traditional PMPs. Existing research (Daniel *et al.* 2015) has highlighted issues with the content of traditional PMPs for people with neuropathic pain, and the findings of the survey presented in Chapter 6, further suggests that more research is required to understand the most appropriate approaches to helping people live well with PDN. For example, research in MS, another complex long-term condition associated with neuropathic pain, suggests that an attitude of pain acceptance was associated with improved patient rating of their quality of life (Harrison *et al.*, 2015a, 2015b). Measures of pain acceptance have never been explored in PDN and would be an avenue for future work.

There was consistency, but not universality, of the impacts that respondents prioritised for improved management. Sleep disturbance was consistently rated the top priority across all the sub-groups analysed. Chapter 6, Table 29 outlined the various subgroups analysed and demonstrates that there were six most frequently identified impacts. Impacts that reflected the subjective pain experience of PDN were not prioritised. This suggests that when presented with options developed from the experience of people with PDN, pain reduction is not necessarily the most important priority for treatment. The clinical implication and future research options of these impacts were discussed in detail in Chapter 7.

Recent research has explored creating a PDN-specific outcome measure (Brod *et al.*, 2015a). This research was partially based on a qualitative study using focus groups and one-to-one interviews conducted by the same research team which was discussed in detail in Chapter 4 (Brod *et al.*, 2015b). The outcome measure development process was informed by the existing literature on PDN impact, and interviews with clinical experts. The Diabetic Peripheral Neuropathic Pain Impact (DPNPI) measure (Brod *et al.*, 2015a) contained three domains: Physical mobility (10 questions), Sleep (5 questions) and Daily activity (3 questions). Clear overlap exists between the impacts prioritised in the Internet survey and the DPNPI outcome measure produced (Brod *et al.* 2015a), both in what was included (sleep, physical function and walking) and what was not. Pain severity was not a priority in the survey nor identified in the DPNPI outcome measure.

Yet pain reduction is the primary outcome in the vast majority of pharmacological trials (Moore, 2013). Secondary outcomes of function and quality of life are usually based on the outcome measures described earlier (Aim 2, Chapter 4), that may not represent the actual issues experienced by people with PDN.

The pilot phase process for this survey suggested it was a challenging, yet achievable process to complete. It was advertised widely on patient focussed social media platforms and by DUK. Respondents had the opportunity to add further impacts. However, despite these attempts to gather a robust sample, the final sample size of n=78 was insufficient to allow the conduct of PCA. PCA would have allowed the clustering together of impacts relating to similar issues (Floyd and Widaman, 1995). The results and discussion presented in Chapter 6 were based on the individual impact statements, if PCA had clustered impacts together, these results and consequent discussion may have been different.

*New knowledge*

- The impacts developed in Aim 2 (Chapter 4) were recognized and endorsed by survey respondents.
- Passive coping approaches were strongly correlated with increased impact load, this was consistent with the wider pain literature (O'Sullivan, 2005).
- Six impacts were prioritised by respondent sub-groups with commonality, but not universality. Sleep was consistently the top priority, others were physical fitness, walking, numb feet, future prognosis and depression.
- Pain severity was not prioritised by survey respondents.

*Future research considerations*

- Clinicians who help people manage PDN must ensure they clearly understand the expectations and priorities of their patients.

## *8.2 Overall thesis limitations and strengths*

### *8.2.1 Limitations of the research*

One limitation of this thesis was the White British profile of the interview and survey samples. This issue has been discussed in the limitations of each study and in the section earlier, but to summarise, the experience of pain is highly contingent on multiple social and cultural variables (Gatchel *et al.*, 2007; Engel, 1978). Research has also found people from ethnic minority groups have additional challenges in self-managing diabetes, including higher levels of social deprivation and reduced health literacy (Claydon, Campbell-Richards and Hill, 2013). This thesis has been based on the experiences of participants who do not represent the full range of cultural variables. For the interview study, participants were located around the UK, but no details of socioeconomic status were recorded. The Internet survey was advertised nationally and on peer-support web pages, these webpages were open to the worldwide web and so respondents may have been based outside the UK. The socio-economic variables of the study populations were not known in detail and so the results and conclusions cannot be assumed to translate to other populations.

Future research conducted in the UK would need to prioritise recruitment of people with PDN from ethnic minority backgrounds. This targeted recruitment would allow checking whether the initial impact codes from the interview study were sufficiently encompassing for the experiences of PDN in all social groups, or whether specific impacts had been overlooked. The results of the Internet survey also require validation in ethnic minority populations with a programme of targeted recruitment.

This thesis has been limited to the UK and so people with PDN were managed within the NHS system. No interview participant described management of diabetes or PDN outside of the NHS in private or independent sector health providers. It is possible that people who are managed within health insurance systems, such as the USA, may have different experiences and perspectives on management of PDN. However, Brod *et al.* (2015b) was conducted in the USA and the impacts identified through their focus groups were broadly similar to those described by participants in this thesis.

A second limitation was that many interviewees, both patients and clinicians not involved in pain management, had little or no actual experience of observing or advising the strategies employed in PMPs. Their perspectives were based only on the PMP mind-map and the ability to ask clarifying questions of the researcher. It was of course important that the researcher did not express opinions based on his own experience of running PMPs. Similarly, the pain specialist clinicians did not share the detailed knowledge about the medical complexity of people with DM, that made their diabetes colleagues more cautious in advocating PMP strategies for PDN.

With more time resource, it would have been useful to arrange cross-discipline visits, for pain clinicians to observe DM clinics, and diabetes clinicians to observe PMPs in progress. This may have altered the clinicians' opinions.

### *8.2.2 Strengths of the research*

The primary strength of this research was that it built upon the experience of people who have lived with PDN for many years. Placing the patient at the centre of both clinical services and research direction aims to ensure that clinical services are accessible and appropriate for the patient cohort (Gooberman-Hill, 2012), and that research focuses on their unmet needs (Brett *et al.*, 2014; Nierse *et al.*, 2012).

The researcher had contact with people living with PDN in the context of interviews, but this was furthered with the help and advice from two EPRPs (Hewlett *et al.*, 2006). The ability to discuss the wording of interview questions, developing codes, theme structures and Internet survey questions helped keep the research grounded and focussed on the experience of living with PDN.

Qualitative research does not expect to generate results that can be generalised beyond the sample population (Polit and Beck, 2010). The limitations in sample population identified in the previous section could have been addressed by devoting project resources to specific recruitment and further qualitative studies. Instead, a decision was made to use the new knowledge, which had been acquired, and explore patient priorities. This decision enabled a form of validation by triangulation (Petty, Thomson and Stew, 2012b; Yardley, 2000). Had many of the impacts generated by the interviews not been rated as experienced by survey respondents, this would suggest there was something unique about the interview sample. As the least frequently experienced impact (*I have contemplated suicide due to my PDN*) was still endorsed by 29.3% of the sample, this suggested the interview sample were at least somewhat representative of other people with PDN.

A further strength of this thesis was the pragmatic approach to the research process, retaining a focus on the patient experience and informed by the clinical experience of researcher and supervisory team. The development of the survey structure to allow respondents to select their priority impacts had a number of potential solutions, each with positives and negatives. It was important to make the process feasible using the online programme, but crucially not to allow any imposition from the researcher to limit the eventual priorities selected by respondents. The options considered and the rational for the approach taken can be found in Chapter 6, section 6.7.

The final strength to highlight was the nature of meetings between researcher and supervisory team, including Amanda, the main EPRP. These meetings were always collegiate, with any differences of opinion clearly voiced and discussed openly, so that all concerned were clear at the end of the meeting, of the rationale for steps taken. The expertise present in these meetings gave confidence, at least to me, that the end results and conclusions of this research process were appropriate and robust.

*8.3 Personal reflections*

I have used research extensively in my clinical practice and when teaching pain related post-graduate courses. In order to give back or contribute to the body of pain rehabilitation knowledge I entered this PhD process hoping to design a series of elegant studies that would clearly answer the specified research questions. Of course, my experience did not match my pre-conceived expectations. But, the experience I have gained of real-world research will be invaluable in my future clinical career.

I was fortunate to spend time observing tertiary care clinics for PDN. I was able to gain a much greater understanding of diabetes and the current management for PDN from these observations. I entered this PhD with insufficient attention to detail. Critical commentary on my written work from the supervisory team, critique that I sometimes felt bordered on pedantry, helped me to reflect more clearly on *precision*. What I initially felt was pedantic was actually a focus on precision in understanding the research paper being appraised, or precision in writing a research proposal. The time devoted by the supervisory team in clinically dissecting my written work, has helped me to reduce the desire to write in academic language, but rather to write in clear and simple English. This has helped me to recognise and structure the argument needed to support a conclusion. I started this PhD as an experienced clinician and the culture shock of being an in-experienced researcher was swift. The supervisory team helped me to navigate this new environment and slowly, gradually managed to help me think more like a researcher.

The biggest regret I have from the PhD process, was not striking the right balance between independent study and asking for support from the supervisory team when required. I could have used the expertise and enthusiasm of the supervisory team more effectively and in a timelier manner. This would be a key piece of advice I would give potential PhD students in the future.

Outside of the studies presented in this thesis, there was family relocation from West Yorkshire back to the South West, moving my family back with my parents for what became a much longer time period than initially expected. My father passed away last year. There were many times when I thought long and hard about why I had started the PhD process in the first place and whether it was worth continuing it to the end. But, Dad would have been disappointed and I am inherently stubborn.

I have been back in part-time clinical practice for two years, and I am aware of the benefits this PhD process has had, and will continue to into the future. I will discuss with the supervisory team the best way to bring the key elements of these research studies to publication, but my future career will not be primarily research focussed. I will continue to develop clinical services that will require on-going monitoring and audit. This PhD has developed my knowledge of the research process required for both quantitative and qualitative studies. It has developed my attention to detail for critical appraisal, argumentation and clarity of writing.

Clinically it has further embedded an approach I endeavour to take with people who have persistent pain for many years, that of open questioning with as few preconceived expectations as possible, of why they have sought physiotherapy. My standard opening question is “What do you want to achieve with this appointment today?” To me this keeps the profession as patient-centred as possible from the first consultation.

These skills and knowledge will enable me to develop further as a clinical physiotherapy leader in the field of pain rehabilitation.

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# Appendices

*Appendix 1 – Published study*

PHYST-826; No. of Pages 9 ARTICLE IN PRESS

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Physiotherapy

Physiotherapy xxx (2015) xxx–xxx

Systematic review

# The role of physical activity and psychological coping strategies in the management of painful diabetic neuropathy – A systematic review of the literature☆

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**Abstract**

**Background** Diabetes is rising in prevalence; painful diabetic neuropathy (PDN) is one complication of diabetes. PDN is primarily managed with medication but analgesic failure is common and people remain in pain and distress. It is unclear whether pain management strategies are appropriate for PDN.
**Objectives** To establish the effectiveness of physical activity and psychological coping strategies for PDN.
**Design** Systematic literature review.
**Data sources** Ten online databases.
**Eligibility criteria (participants and interventions)** Controlled trials reporting specific results for PDN, investigating, (a) physical activity or (b) psychological coping strategies and measuring pain as an outcome. The search was restricted to published research with no restriction on language or date of publication.
**Study appraisal methods** Methodological quality and risk of bias assessed with Cochrane collaboration and NICE checklist for randomised controlled trials.
**Results** Of 1306 titles identified, four studies met the inclusion criteria. Two trials investigated physical activity and two investigated psychological coping interventions. Studies showed pain measures improved or did not worsen compared to controls, but methodological quality was moderate and results need cautious interpretation.
**Limitations** The studies were of small sample size and used a diverse range of outcome measures. There is high risk of bias from lack of blinding and attrition at follow up.
**Conclusions and implications of key findings** The research literature in this area is sparse and inconsistent, despite the pressing clinical challenge of PDN. Firm conclusions cannot be drawn from the studies included. Further high quality research is required to match treatment provision to patient requirements.


*Keywords:* Diabetes; Pain; Physical activity; Psychological coping; Systematic literature review

## Introduction

Diabetes mellitus (DM) is an increasingly common endocrine disorder, the prevalence of which is rising due to rising levels of obesity, decreasing physical activity and an ageing population [1]. As management strategies for DM

☆ PROSPERO registration number: CRD42013006365.
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0031-9406/

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*Appendix 2 – Data extraction table*

| Author | Year | Evidence of PDN diagnosis | PA or psych | Study design | Nature of intervention | Psych target of intervention | Nature of physical activity | Intensity and frequency | Participants intervention | Participants control | Lost to follow up | Adherence | Details of control arm | Duration of follow up | Outcome measure | Results | Adverse events |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ahn | 2012 | | | | | | | | | | | | | | | | |
| Dixit | 2014 | | | | | | | | | | | | | | | | |
| Otis | 2013 | | | | | | | | | | | | | | | | |
| Teixeira | 2010 | | | | | | | | | | | | | | | | |

*Appendix 3 – Patient interview study PIS*

**Research Study Title:** Qualitative exploration of living with and managing painful diabetic neuropathy.

You are being invited to take part in a study. Before you decide if you want to take part, it is important for you to understand why the study is being done and what it will involve. Please take the time to read the following information carefully. Talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

**What is the purpose of the study?**

This study is part of a series of studies, aiming to improve ways of managing painful diabetic neuropathy (PDN).

This study involves face-to-face interviews with people who experience PDN.

The topics of this interview will include:

- How the PDN impacts on your life.
- How you currently manage the PDN and its impact.
- How would you view physical activity as a strategy to manage the PDN.
- How would you view strategies used for the management of other chronic pain problems.
- How you prioritise the competing demands of managing diabetes and its complications.

**Do I have to take part?**

It is up to you to decide if you want to take part. If, once you have read this information sheet, you are still interested in this study and would like to know more please contact Ben Davies by using the pre-paid reply slip at the beginning of this information. If you do agree to take part, you will be asked to sign a consent form when you attend for the interview. You are free to withdraw at any time, without giving a reason. Your usual clinical care for the diabetes and for PDN is unaffected by your participation in this research.

**Why have I received this information?**

The research is about diabetes and a pain condition that occurs in some people who have diabetes (Painful Diabetic Neuropathy). Your diabetic clinical team have diagnosed you with both of these conditions and therefore we would like to know more about your experiences so that we can design an intervention to potentially help people like you in the future.

**What will the research involve?**

If you have an initial interest in being involved with this research, please contact me using the pre-paid reply slip at the beginning of this information. I will contact you to answer any questions you have, and to discuss being involved in this study. If you are happy to participate we will schedule a one off interview, this will be face to face and can be at your home, your local GP surgery or at another place that is convenient to you.

The interview will take no longer than 90 minutes.

Before we meet, I will ask you to look at a list of possible complications that diabetes can cause, the list is at the end of this information sheet. I will ask you to identify which of these problems you have and to rank the order in which they impact on how you live your life. If you agree to take part in the research I will ask you to bring this sheet to the interview.

When we meet, I will answer any further questions that you may have. If you agree to participate I will ask you to give written consent to be involved and for me to record the interview.

Some basic information will be recorded including age, gender, ethnicity, type of diabetes, duration of diabetes and pain, and a list of the painkillers that you use.

I will use this information to ensure that I recruit a wide range of people who experience this problem.

I will send you a written copy of the interview to allow you to check the accuracy.

**What are the risks and benefits of taking part?**

I will be asking you to describe in detail how your pain impacts on your life. This maybe distressing for you and for this reason you can choose to terminate the interview or take a break at any time. Should the interview cause significant distress I will be able to put you in touch with Professor McCabe in order to plan the best way forward.

There are no immediate benefits to participating, but in the long term this research will hopefully lead to better management of PDN.

**What happens when the research study stops?**

The data collected will be analysed and a report will be written. A summary report will be made available to you on request. This data will be used to define a pain coping skills programmes specifically for PDN. The University of the West of England (UWE) will keep the anonymous data for 9 years.

**Will my taking part in the study be kept confidential?**

Yes, I will anonymise the interview transcripts and research data, and you will not be referred to by name in the interview. All electronic files will be stored on secure password protected servers at UWE Bristol. All paper files will be anonymised and stored in locked filing cabinets at UWE Bristol. All identifying information will be removed when the data is written up for publication.

**What will happen if I don't want to carry on with the study?**

If you decide you do not wish to carry on with the study you may withdraw at any time. Any data that we have collected up to your withdrawal will not be used in the study. Your usual clinical care will not be affected by taking part in this study even if you subsequently decide to withdraw.

**Who is organising the study?**

This study forms part of a PhD research project at UWE.

The study has been reviewed by UWE Ethics committees and local NHS Research Ethics Committees.

**Chief Investigator:**

Ben Davies, MSc, MCSP, PhD candidate.

**PhD supervisory team:**

Professor Candy McCabe, UWE.

Dr Fiona Cramp, UWE.

Dr Jeremy Gauntlett-Gilbert, RNHRD.

Professor David Wynick, UHBristol.

*Appendix 4 – Clinician interview study PIS*

**Research Study Title:** Clinicians' perspectives on the management of painful diabetic neuropathy

You are being invited to take part in a study. Before you decide if you want to take part, it is important for you to understand why the study is being done and what it will involve. Please take the time to read the following information carefully. Talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

**What is the purpose of the study?**

This study is part of a series, aiming to enhance management strategies for painful diabetic neuropathy (PDN).

This study involves interviews (face to face or via telephone) with clinicians who are involved in the management of diabetes and PDN. The focus of the interview will be to obtain: 1) your views on current management strategies for PDN, and 2) your views on pain coping skills programmes strategies and their application to PDN.

**Do I have to take part?**

It is up to you to decide whether you want to take part. If, once you have read this information sheet, you are still interested in this study and would like to know more please contact Ben Davies via the email or phone number provided at the end of this document. If you do agree to take part, you will be asked to either sign a consent form when you attend for the interview appointment, or give verbal recorded consent if the interview is by telephone. You are free to withdraw at any time, without giving a reason.

**Why have I received this information?**

I plan to interview members of all professions who help manage diabetes and PDN. This includes a representative sample of all members of the multi disciplinary teams in secondary and primary care. I hope to recruit medical staff, specialist nurses, practice nurses, dieticians, podiatrists, psychologists, occupational therapists and physiotherapists.

You have received this study information because I believe that you fulfil these criteria.

**What will the research involve?**

If you are willing to participate I will schedule a one off interview appointment, this can be face to face or via telephone. The interview will take no longer than an hour.

When we meet, I will answer any further questions that you may have. If you agree to participate I will take informed consent from you to be involved and to record the interview. If the interview is by phone, consent will be the first recorded section.

With your permission the interview will be recorded to digital audio file and transcribed.

The areas of interest for this interview will include:

- Your profession and duration of experience with diabetes and PDN.
- How you currently manage PDN.
- Your views on physical activity as a strategy for the management of PDN.
- Your views on strategies from pain coping skills programmeto manage PDN.
- Your view on how patients would respond to the offer of a PDN-specific pain coping programme.
- Any practical suggestions for the implementation of a potential PDN-specific pain coping programme.

I will send you a copy of the transcript following the interview to allow you to comment on the accuracy. All the interview transcripts will be analysed to look for themes that would help inform a PDN specific pain coping skills programme.

**What are the risks and benefits of taking part?**

There are no immediate risks or benefits to participants taking part in this research. You will however need to give up around 1 hour of your time in order to take part.

**What happens when the research study stops?**

The data collected will be analysed and a report will be written. A summary report will be made available to you on request. I will use this data to inform an intervention specific for PDN.

**Will my taking part in the study be kept confidential?**

Yes, your involvement in this study will not be revealed to anyone. Further, the audio transcriptions will be anonymised and you will not be referred to by name in the interview. All electronic files will be stored on secure password protected servers at UWE Bristol. All paper files will be anonymised and stored in locked filing cabinets at UWE Bristol. All identifying information will be removed prior to publication.

**What will happen if I don't want to carry on with the study?**

If you decide you do not wish to carry on with the study you may withdraw at any time. Any data that we have collected up to your withdrawal will not be used in the study.

**Who is organising the study?**

This study forms part of a PhD research project at UWE.

This study has been reviewed by UWE Faculty Ethics Committees.

**Chief Investigator:**

Ben Davies, MSc, MCSP, PhD candidate.

**PhD supervisory team:**

Professor Candy McCabe, UWE.

Dr Fiona Cramp, UWE.

Dr Jeremy Gauntlett-Gilbert, RNHRD.

Professor David Wynick, UHBristol.

*Appendix 5 – Patient interview questionnaire*

If you enrol in the study, please complete this questionnaire and bring it with you to the interview.

Diabetes can cause a range of complications.

These complications are arranged on this page, in no specific order.

Please circle the complications that you experience

Please note next to each complication how you would rank each complication in terms of how much it interferes with your life, with 1 = Most interfering problem, 2 = Next most interfering etc. etc.

Eye problems

Kidney problems

Memory loss

"Frozen Shoulder"

"Fatty Liver" problems

Nerve pain

Numbness

Heart/Vascular problems

Sex life problems

High blood pressure

Bladder problems

Foot ulcers

Blood sugar control problems

Bowel problems

Weight issues

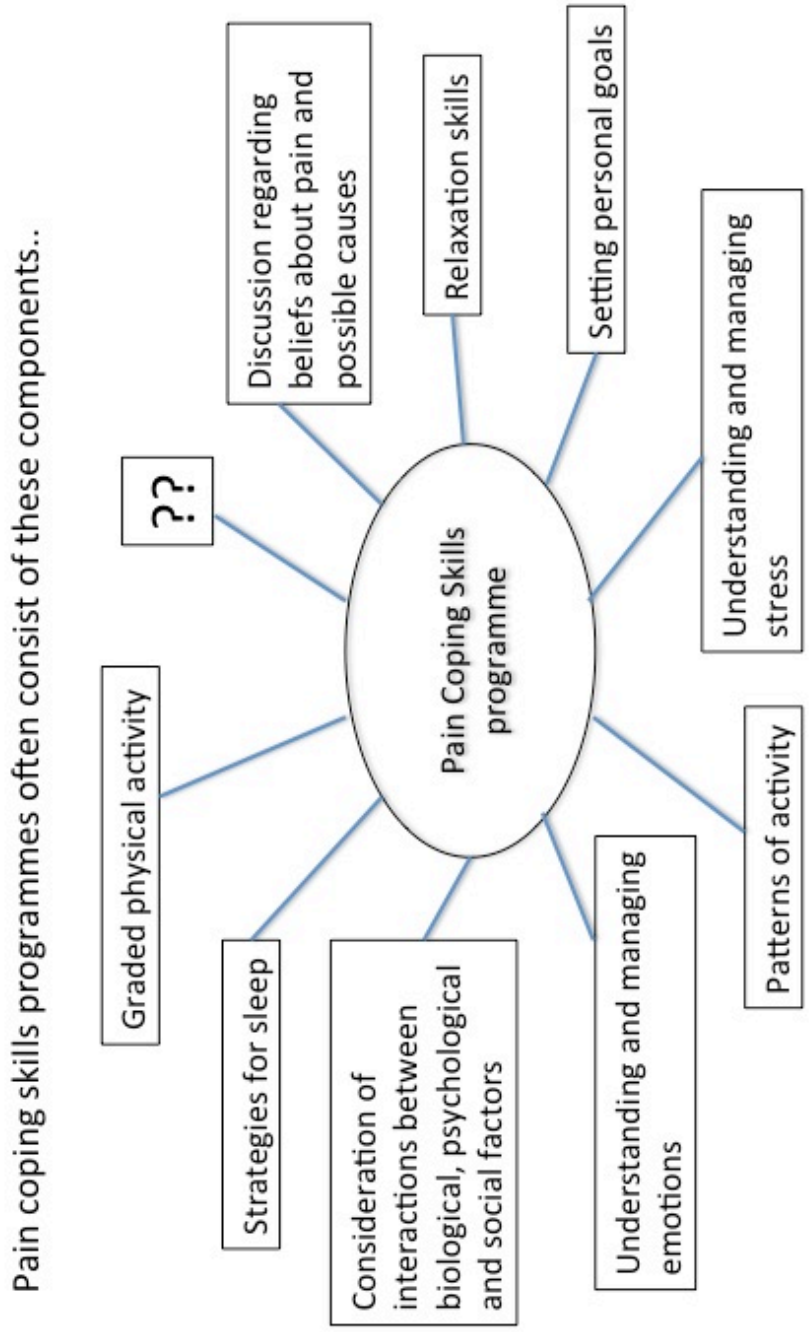
Mood or emotional problems

Any other problems not listed?

_____

_____

*Appendix 6 – Pain management programme mind-map*



*Appendix 7 – Patient Interview consent form*

Consent form date of issue: 28/5/13
Consent form version number: v2
REC Ref: 013/SW/0125

Patient Identification Number for this trial:

**CONSENT FORM**

Title of Project: **Patient perspectives on management of painful diabetic neuropathy**

Name of Researcher: **Ben Davies**

Please initial all boxes

1. I confirm that I have read and understand the information sheet dated 28/5/13 (version 4.3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason. ☐

3. I understand that this interview will be audio recorded ☐

4. I understand that research data, including interview recordings will be stored anonymously ☐

5. I agree to take part in the above study. ☐

| Name of Participant | Date | Signature |
|---|---|---|
| Name of Person | Date | Signature |

*Appendix 8 – Patient demographics form*

Patient Identification Number for this trial:

---

**DEMOGRAPHIC FORM**

---

Title of Project: **Patient perspectives on management of painful diabetic neuropathy**

Name of Researcher: **Ben Davies**

Gender

Age

Ethnicity

DM type

Duration of DM

Duration of PDN

Analgesia

Occupational status

*Appendix 9 – Patient interview schedule*

| Main root question | Possible stem questions |
|---|---|
| Please tell me about your life with PDN? | • Tell me more about how it affects your working day?<br>• Can you elaborate on how it affects your social life?<br>• In what ways do others close to you support you in managing this problem? |
| How do you currently manage this pain problem? | • Tell me more about the benefits of the medication/side effects of the medication?<br>• Tell me more about the non-medication ways you use to minimise the impact of PDN |
| With other chronic pain problems, maximising function through graded activity as a key strategy, how does this sound in relation to your PDN? | • If pain increases with activity – what thoughts do you have?<br>• What images do you have when pain increases?<br>• Can you explain what you feel is happening in your feet, when the pain increases? |
| Pain coping skills courses use the strategies outlined in this diagram to help maximise quality of life – can we talk through how they may relate to your PDN? | • Tell me more how you think [relaxation, challenging negative thoughts, sleep strategies, communication skills training, graded activity] may or may not be of benefit to your management of PDN?<br>• What practicalities need to be considered for a PDN coping skills programme? |

*Appendix 9b – Clinician interview schedule*

The interview schedule will be developed in an iterative manner across the first 3-5 interviews. The initial schedule will be as follows:

1. Profession and years experience with DM and PDN (structured)
2. When patients describe that they have PDN as a complication of their DM, what management options do you currently have?
3. What are your views on physical activity as a strategy to manage PDN?
4. What are your views on pain coping skills programme strategies to manage PDN?
5. How do you think patients would respond to the offer of a PDN specific coping skills programme?
6. Do you have any practical suggestions for the implementation of a potential PDN specific pain coping skills programme?

Questions 2-6 will be semi structured, the interviewer will follow up points of interest with the participant.

*Appendix 10 – Patient interview UWE Ethical approval*

University of the West of England
BRISTOL

Faculty of Health & Life Sciences
Glenside Campus
Blackberry Hill
Stapleton
Bristol BS16 1DD
Tel: 0117 328 8487

Our ref: JMA/lt

26 April 2013

Ruth Avery
South West - Frenchay
Bristol REC Centre
Level 3, Block B
Whitefriars
Lewins Mead
Bristol BS1 2NT

Dear Ms Avery

**Re: Qualitative exploration of living with and managing PDN**

**Chief investigator: Benjamin Davies**

**Ref No: 13/SW/0125**

I am writing to confirm that the University of the West of England, Bristol ("UWE") has agreed to act as Research Sponsor in accordance with the Department of Health Research Governance Framework (2001) for the above research. UWE's acceptance of Research sponsorship is subject to ethics approval having been obtained.

UWE has made the following insurance arrangements for employees, and for students working under the supervision of a UWE employee, and where the project is included on an authorised UWE research register.

UWE has insurance cover for clinical trials up to £5m in the aggregate which includes cover for non-negligent harm. This cover is provided only when UWE (via Research, Business and Innovation) has approved projects with our insurers and they are then listed on our clinical trials register.

For research which is not deemed a clinical trial (i.e. not on UWE's clinical trials register):

- UWE's Professional Indemnity policy provides insurance cover for indemnity against legal liability for damages and claimant's costs and expenses arising out of any act, neglect, error or omission.

- UWE's Employers Liability Insurance is in place to protect UWE's employees if they are harmed whilst engaged on UWE business, should UWE be held legally liable.

- UWE's Public Liability insurance policy covers legal liability for third party personal injury, death, disease or illness to any person or loss or damage to third party property.

Details of the Employers/Public and Professional Indemnity policy covers are attached.

Yours sincerely

**Prof Jennifer M. Ames**

Associate Dean (Research and Innovation)

Encl

*Appendix 11 – Patient interview R&D approval*

University Hospitals Bristol NHS
NHS Foundation Trust

Mr Ben Davies
Blue Lodge (Post Graduate)
Glenside Campus
Blackberry Hill
BS16 1DD

Research and Innovation
University Hospitals Bristol NHS Foundation Trust
Education & Research Centre Level 3
Upper Maudlin Street
Bristol BS2 8AE

Tel: 0117 342 0233
Fax: 0117 342 0239

email: research@uhbristol.nhs.uk

website: http://www.uhbristol.nhs.uk/research-innovation

**12/08/2013**

**NHS Permission for Research has been granted for the study detailed below at University Hospitals Bristol NHS Foundation Trust (UHBristol). Permission is subject to any conditions and is effective from 12/08/2013 until 01/04/2014.**

Dear Mr Davies,

**RE: Qualitative exploration of living with and managing PDN (ME/2013/4345).**

NHS permission for the above research has been granted on the basis of the application submitted and a favourable opinion from an authorised REC.

Permission is granted on the understanding that the study is conducted in accordance with the Research Governance Framework, Good Clinical Practice, and NHS Trust policies and procedures available at http://www.uhbristol.nhs.uk/research-innovation/are-you-a-researcher/information-for-researchers/post-approval/ As Principal Investigator it is your responsibility to ensure you and your team are familiar with relevant research related policies and procedures; these can be found at http://www.uhbristol.nhs.uk/research-innovation/research-and-innovation-department-at-uh-bristol/

**It is also a condition of NHS Permission at this site that local recruitment data is uploaded to the EDGE system and the study record is kept up-to-date. Please contact the Research Management Office if you are unsure how to do this.**

**The following conditions must be met prior to recruitment commencing:**

• A site file is set-up and delegation log established

UHBristol is required to monitor research to ensure compliance with the Research Governance Framework and other legal and regulatory requirements. For further details about monitoring arrangements please contact the Research Management Office. The Research Management Office will monitor recruitment on an on-going basis and can provide support and advice if you are experiencing problems in meeting your targets within the agreed time frame.

University Hospitals Bristol NHS
NHS Foundation Trust

The Research Management Office should be notified of any urgent safety measure taken in order to protect research participants against any immediate hazard to their health or safety. This should be within the same time frame as notification to the REC and any other regulatory bodies and should include the reasons why the measures were taken and any plan for further action.

NHS indemnity is provided for the period of permission given above. Requests for changes to the period of permission (eg an extension of the study) must be made to the Research Management Office before permission ceases with an explanation as to why the change is being sought.

All amendments (including changes to the local research team) need to be submitted in accordance with regulatory and national requirements which can be found on IRAS. The Research Management Office also needs to be notified if there are any changes to the study status.

We wish you every success with this study.

Yours sincerely

Diana Benton
Acting Head of Research and Innovation/Deputy Director of Research

**Copy to:**

**Professor Candy McCabe, Royal National Hospital for Rheumatic Diseases.**

**Mrs Leigh Taylor, University of the West of England.**

*Appendix 12 – NHS REC committee approval*

NHS
Health Research Authority
**NRES Committee South West - Frenchay**
Bristol Research Ethics Committee Centre
Level 3, Block B
Whitefriars
Lewins Mead,
Bristol
BS1 2NT

Telephone: 01173421334
Facsimile: 01173420445

24 May 2013

Mr Ben Davies
PhD candidate
University of the West of England
Blue Lodge (Post Graduate)
Glenside Campus
Blackberry Hill
BS16 1DD

Dear Mr Davies

**Study Title:** **Patients' perspective on the management of painful diabetic neuropathy**
**REC reference:** **13/SW/0125**
**IRAS project ID:** **124520**

The Research Ethics Committee reviewed the above application at the meeting held on 10 May 2013.

**Documents reviewed**

The documents reviewed at the meeting were:

| *Document* | *Version* | *Date* |
|---|---|---|
| Covering Letter | | 29 April 2013 |
| Evidence of insurance or indemnity | | 05 February 2013 |
| Investigator CV | | |
| Letter from Sponsor | | 29 April 2013 |
| Letter of invitation to participant | 1 | 18 April 2013 |
| Other: Supervisor McCabe CV | | |
| Other: Supervisor Dr Gauntlett-Gilbert CV | | |
| Other: Supervisor Dr Cramp Cv | | |
| Other: David Wynick CV | | |
| Participant Consent Form | 1 | 11 February 2013 |
| Participant Information Sheet | 4.2 | 18 April 2013 |

| | | |
|---|---|---|
| Protocol | 4.2 | 18 April 2013 |
| REC application | | 24 April 2013 |

**Provisional opinion:**

The Committee is unable to give an ethical opinion on the basis of the information and documentation received so far. Before confirming its opinion, the Committee requests that you provide the further information set out below.

Authority to consider your response and to confirm the Committee's final opinion has been delegated to the Chair.

**Further information or clarification required:**

1. Participant Information Sheet (PIS) requested changes:

- To detail who is going to anonymise the data.

- A sentence on informing Professor Mccabe about distress in a participant and then discussing this with Professor McCabe be included in the PIS.

2. Consent form requested changes:

- Needs to include a section regarding permission to record the interview.

- To store anonymous data including the recordings to be included.

3. Please provide clarification in a covering letter to the Committee who the EPRP is and provide a copy of their CV.

4. Please provide a specific end date of the study.

5. The form on which data is being collected to be submitted for review.

6. Please provide clarification in a covering letter as to who is purposively sampling and at what stage in the study will this sample be taken.

7. Please provide clarification in a covering letter who is collecting the demographic data and who will be reviewing this.

8. Please provide clarification in a covering letter regarding the exclusion criteria detailed in A17-2 of the IRAS form, how was the pain going to be assessed and would this be done with the use of pain scores.

9. Please provide clarification in a covering letter if any verbal consent will be taken, and if so this would not be appropriate and only written consent should be sort.

10. Please provide clarification in a covering letter as to why the clinician cannot give out the PIS and Consent form with a study contact number/email address so that potential participant can contact the researcher. (This would avoid the need for obtaining consent under point 9).

11. Please provide clarification in a covering letter if the choice of interviewing venue has been agreed with the GPs for this to be an option.

12. Please provide clarification in a covering letter if you and the ERPR would know the participants.

13. Please provide clarification in a covering letter as to who would be transcribing the data and reassurance there would not be chance of participant identification.

**If you would find it helpful to discuss any of the matters raised above or seek further clarification from a member of the Committee, you are welcome to contact Christine Hobson 0117 342 1334.**

When submitting your response to the Committee, please send revised documentation where appropriate underlining or otherwise highlighting the changes you have made and giving revised version numbers and dates.

If the committee has asked for clarification or changes to any answers given in the application form, please do not submit a revised copy of the application form; these can be addressed in a covering letter to the REC.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 23 June 2013.

**Membership of the Committee**

The members of the Committee who were present at the meeting are listed on the attached sheet.

There were no declarations of interest.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

| **13/SW/0125** | **Please quote this number on all correspondence** |
|---|---|

Yours sincerely

**Dr Robert Beetham**
**Chair**

Email: nrescommittee.southwest-frenchay@nhs.net

*Appendix 13 – REC substantial amendment*

**Membership of the Committee**

The members of the Committee who took part in the review are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

| **13/SW/0125:** | **Please quote this number on all correspondence** |
|---|---|

Yours sincerely

P.P.

**Dr Robert Beetham**
**Chair**

E-mail: nrescommittee.southwest-frenchay@nhs.net

*Enclosures:* *List of names and professions of members who took part in the review*

*Copy to:* *Mrs Diana Benton, University Hospitals Bristol NHS Foundation Trust*
*Mrs Leigh Taylor*

Research Ethics Committee established by the Health Research Authority

*Appendix 14 – Clinician permission letters*

North Bristol NHS Foundation Trust

**Title: Clinicians' perspectives on the management of painful diabetic neuropathy**

**CI: Ben Davies**

**R&D Reference: 3164**

**Start Date: 19 June 2013**

**End Date: 01 September 2013**

I am pleased to confirm North Bristol NHS Trust (NBT) NHS permission for the above study.

**FULL R&D APPROVAL**

**You have permission to begin recruitment**

I understand that the University of the West of England will act as sponsor for this study.

We acknowledge that this project does not require ethical review by a NHS Research Ethics Committee under the UK Health Departments' Governance Arrangements for Research Ethics Committees (GAfREC), however it may be necessary to contact the University Research Ethics Committee (UREC).

We wish you every success with your study. We are keen to support good research at North Bristol NHS Trust and are pleased that you have decided to conduct your project here.

The lead Research Governance Officer for this study is Joanna Strickland, who will remain your ongoing main point of contact. They can be reached at the following email address: Joanna.strickland@nbt.nhs.uk

Approval is given on the understanding that this project be carried out according to Good Clinical Practice and UK Statutory Instrument, and within the guidelines of the NHS Research Governance Framework for Health and Social Care, and NHS Trust policies, procedures, and SOPs which are available online at http://www.nbt.nhs.uk/research.

In particular you have responsibility for:

- Ensuring that, all participants sign informed consent (whenever applicable).
- Adhering to the protocol and ensuring your co-workers do the same.
- Ensuring all recruitment figures are uploaded to the Edge database on a weekly basis.
- Providing us with information about any amendments to the protocol, changes in funding, personnel or end date.
- Informing us of any research-related adverse events.
- Ensuring that any staff working on this study at this site have been issued with a contract with NBT (honorary, substantive or bank) or a letter of access before they commence work on the study at this site.
- Maintenance of an Investigator Site File and/or Trial Master Files.

Researchers who hold substantive or honorary contracts with North Bristol NHS Trust (NBT) will be covered against claims of negligence by patients of NBT under the Clinical Negligence Scheme for Trusts (CNST). This scheme does not cover 'no fault' compensation and the Trust is precluded from taking out separate insurance to cover this. Any patient or volunteer taking part in the study is entitled to know that if they suffered injury as a result of participating in the study they would first have to prove negligence in a court of law before they could gain compensation. If the study

involves patients of any other Trust or healthcare organisation, you will need to confirm the indemnity arrangements with that organisation.

In addition, other information may be requested from time to time and lay summary of the results will be requested from you at the end of the study.

This full R&D approval document will need to be filed in your Investigator Site File and/or Trial Master Files.

In accordance with the NBT Research Monitoring and Audit policy, this study is subject to audit by the R&I Office. We will contact the Principal Investigator to make appropriate arrangements for this.

Many thanks

**Nicola Williams**

**Deputy Director**

**Research & Innovation**

**North Bristol NHS Trust**

**University Hospital Bristol NHS Foundation Trust**

University Hospitals Bristol NHS
NHS Foundation Trust

Mr Ben Davies
University of the West of England
Blue Lodge (Post Graduate)
Glenside Campus
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BS16 1DD

Research and Innovation
University Hospitals Bristol NHS Foundation Trust
Education & Research Centre Level 3
Upper Maudlin Street
Bristol BS2 8AE

Tel: 0117 342 0233
Fax: 0117 342 0239

email: research@uhbristol.nhs.uk

website: http://www.uhbristol.nhs.uk/research-innovation

**30/04/2013**

**NHS Permission for Research has been granted for the study detailed below at University Hospitals Bristol NHS Foundation Trust (UHBristol). Permission is subject to any conditions and is effective from 30/04/2013 until 01/09/2013.**

Dear Mr Davies,

**RE: Clinicians' perspective on the management of painful diabetic neuropathy, ME/2013/4340.**

NHS permission for the above research has been granted on the basis of the application submitted and a favourable opinion from an authorised REC.

Permission is granted on the understanding that the study is conducted in accordance with the Research Governance Framework, Good Clinical Practice, and NHS Trust policies and procedures available at http://www.uhbristol.nhs.uk/research-innovation/are-you-a-researcher/information-for-researchers/post-approval/ As Principal Investigator it is your responsibility to ensure you and your team are familiar with relevant research related policies and procedures; these can be found at http://www.uhbristol.nhs.uk/research-innovation/research-and-innovation-department-at-uh-bristol/

**It is also a condition of NHS Permission at this site that local recruitment data is uploaded to the EDGE system and the study record is kept up-to-date. Please contact the Research Management Office if you are unsure how to do this.**

**The following conditions must be met prior to recruitment commencing:**

• A site file is set-up and delegation log established

UHBristol is required to monitor research to ensure compliance with the Research Governance Framework and other legal and regulatory requirements. For further details about monitoring arrangements please contact the Research Management Office. The Research Management Office will monitor recruitment on an on-going basis and can provide support and advice if you are experiencing problems in meeting your targets within the agreed time frame.

University Hospitals Bristol NHS
NHS Foundation Trust

The Research Management Office should be notified of any urgent safety measure taken in order to protect research participants against any immediate hazard to their health or safety. This should be within the same time frame as notification to the REC and any other regulatory bodies and should include the reasons why the measures were taken and any plan for further action.

NHS indemnity is provided for the period of permission given above. Requests for changes to the period of permission (eg an extension of the study) must be made to the Research Management Office before permission ceases with an explanation as to why the change is being sought.

All amendments (including changes to the local research team) need to be submitted in accordance with regulatory and national requirements which can be found on IRAS. The Research Management Office also needs to be notified if there are any changes to the study status.

We wish you every success with this study.

Yours sincerely

Diana Benton
Acting Head of Research and Innovation/Deputy Director of Research

**Copy to:**

**Professor Wynick**

**Professor McCabe**

**Mrs Taylor**

*Appendix 15 – Patient interviewee details*

| Identifier | Pseudonym | Interview | Gender | Age | Ethnicity | DM type | DM duration | PDN duration | Occupation |
|---|---|---|---|---|---|---|---|---|---|
| S1P01 | Mary | H | F | 44 | WB | 1 | 36 | 7 | medically retired |
| S1P02 | Anne | H | F | 52 | WB | 2 | 20 | 15 | medically retired |
| S1P03 | John | U | M | 69 | WB | 1 | 50 | 15 | medically retired |
| S1P04 | Joan | NHS/H | F | 57 | WB | 2 | 10 | 10 | medically retired |
| S1P05 | Bob | U | M | 63 | WB | 2 | 23 | 6 | medically retired |
| S1P06 | Mike | U | M | 65 | WB | 2 | 7 | 5 | retired |
| S1P07 | Sally | H | F | 48 | WB | 1 | 24 | 8 | employed |
| S1P08 | Ellen | H | F | 63 | WB | 2 | 18 | 6 | medically retired |
| S1P09 | Barbara | P | F | 80 | WB | 2 | 22 | 14 | retired |
| S1P10 | Neil | P | M | 66 | WB | 1 | 34 | 20 | retired |
| S1P11 | Aaron | P | M | 75 | WI | 2 | 10 | 4 | retired |
| S1P12 | Mark | P | M | 62 | WB | 2 | 30 | 13 | medically retired |
| S1P13 | Philip | P | M | 57 | WB | 1 | 30 | 20 | medically retired |
| S1P14 | Daniel | P | M | 67 | WB | 1 | 38 | 10 | retired |
| S1P15 | Clive | P | M | 86 | WB | 2 | 12 | 3 | retired |
| S1P16 | Sam | P | M | 53 | WB | 1 | 42 | 13 | volunteer |
| S1P17 | Sarah | P | F | 24 | WB | 1 | 18 | 1 | employed |
| S1P18 | Heather | P | F | 57 | WB | 2 | 8 | 10 | medically retired |
| S1P19 | Lisa | H | F | 69 | WB | 2 | 20 | 10 | retired |
| S1P20 | Roger | P | M | 86 | WB | 2 | 10 | 1 | retired |
| S1P21 | Kate | P | F | 58 | WB | 1 | 24 | 14 | medically retired |
| S1P22 | Dawn | P | F | 68 | WB | 1 | 48 | 24 | retired |
| S1P23 | Jane | P | F | 68 | WB | 2 | 7 | 9 | retired |
| (Interview) Location: H – home, U – University campus, NHS – NHS premises, P – phone, 1 – Type 1 diabetes, 2 – Type 2 diabetes, WB – White British, WI – West Indian. | | | | | | | | | |

*Appendix 16 – Partial transcript of patient interview*

**The partial transcripts included in appendix 16 and 17 have not been edited from the verbatim transcripts.**

INTERVIEWER:

So how did you cope then, how, you've had this problem now for ten years, you take occasional co codamol?

LISA:

When I have a really bad day I give in to it and don't try and do too much, um and then make up for it when I've got a good day.

INTERVIEWER:

Um.

LISA:

Um I mean it's never lasts all day, I mean it's there, it's there in the background, I mean my feet are hurting now, but I've learnt to live with it, so I just sort of basically ignore it, um, when it's really bad I wouldn't walk very far.

INTERVIEWER:

Uh huh.

LISA:

This is the biggest impact, um, I used to go, believe it or not, I used to go to exercise classes, or originally used to go to a gym regularly.

INTERVIEWER:

Um.

LISA:

Um and then when I started getting bad, I stopped and used to go to um a weekly, twice a week an exercise class, but then because they got really quite bad, I felt my balance wasn't good and my stability or my feet wasn't good, so I was afraid of falling over in that, in that sort of, so basically gave up doing that, so I, it's hard to explain, um, because you felt un, un, insecure, er you stopped and now I sort of feel I don't know what I could and couldn't do that wouldn't make it worse.

INTERVIEWER:

Um.

LISA:

If that sounds logical to you?

INTERVIEWER:

What kind of physical activity could you do?

LISA:

Could I do that would not make things worse?

INTERVIEWER:

Yeah.

LISA:

Um.

INTERVIEWER:

And you'd also want to be safe with this?

LISA:

And safe that, that's the other thing yes.

INTERVIEWER:

Loss of balance and sensitivity?

LISA:

Yes I was losing a bit of sensation on the feet, so um sort of standing up in a, in a open space and sort of say moving from foot to foot, you felt that you were unstable and so that really drove me to really stop doing that.

INTERVIEWER:

Uh huh.

LISA:

So really the only physical exercise now is I do the gardening or the housework or walking.

INTERVIEWER:

Uh huh.

LISA:

But I don't do anything that would involve me sort of standing on one leg or something, whereas I might lose um the sort of balance.

INTERVIEWER:

Yeah so you're being somewhat safe?

LISA:

Yes, yes, try to be safe, I mean it's always something that, is very difficult to think about how you get back to doing some exercise without um somebody telling you that yes you should sit and do, so I mean, I do sit and do some exercising of my feet when I'm sitting down at times.

INTERVIEWER:

You sort of do like the ankle rolls and up on the toes and things?

LISA:

Yes, and, and try to keep the muscles going there, but I'm sure that I'm not doing all I should do or couldn't do, but I don't know what else to do.

INTERVIEWER:

Um.

LISA:

If that makes sense [laughing].

INTERVIEWER:

Yeah absolutely so you said you have, you rarely take medication you just kind of get on with this problem?

LISA:

Yes, yes.

INTERVIEWER:

And you seem to suggest that on, you know, a day when your pain is particularly bad, you'll do less?

LISA:

I adapt to what I'm doing for the day yes.

INTERVIEWER:

Your expectations for that day will drop?

LISA:

Yes.

INTERVIEWER:

But then you'll catch up when things improve?

LISA:

Well being retired, I mean, if, if I don't need to go shopping today and if my feet are bad, then I go shopping tomorrow.

INTERVIEWER:

Um.

LISA:

Um you know, if, if it's a nice, if a garden needs to do a bit, and we, we feel like doing it fine, but if I don't, then I don't, um, and it's because of the, I am now retired, obviously, um I've got that flexibility in life, um, so yes, I cope that way.

INTERVIEWER:

So those time pressures are different?

LISA:

The time pressures are different, if I was at work it would be completely different.

INTERVIEWER:

Um.

LISA:

Um and then you'd have to be trying to go somewhere when you felt you were sort of crippled.

INTERVIEWER:

Uh huh.

LISA:

But it doesn't.

INTERVIEWER:

Any other practical strategies you have for managing this impact?

LISA:

Shout a bit [laughing], I've got a very good husband, he's very good [laughing].

INTERVIEWER:

He understands?

LISA:

Er yeah, yeah, I mean if they are bad, he will, you know, he helps around the house, so if I can't do something, he'll do it.

INTERVIEWER:

Uh huh.

LISA:

So um, apart from that, I just, I'm just me and just sort of try to get on with things and try not to let it sort of wallow in self pity and depression and um just try and be me, just get on with life.

*Appendix 17 – Partial transcript of clinician interview*

INTERVIEWER:

Okay and for going through that process of managing that patient, other than the pain scale, the kind of one to ten scale of pain …

GP1:

Yeah.

INTERVIEWER:

… is there anything else that you consider in your assessment about the patient?

GP1:

Yeah, I mean as I would with any type of chronic pain whether it was back pain or anything else …

INTERVIEWER:

Yeah.

GP1:

erm, of course it's really important to look at the psychological aspects because two people can have apparently the same pathological or an anatomical problem …

INTERVIEWER:

Yeah.

GP1:

but they will perceive pain in very different ways, so you know I'd have to think about are they depressed …

INTERVIEWER:

Yeah.

GP1:

if they're depressed then that will make them, the chances are it makes pain worse and …

INTERVIEWER:

Yeah.

GP1:

look at other reasons why they're, why they maybe feeling pain.

INTERVIEWER:

Do you use any questionnaires in that process or is it just a consultation, you know conversation etcetera?

GP1:

Well if its depression then its a conversational thing and then if I'm …

INTERVIEWER:

Sure.

GP1:

suspicious then we, on a bog standard thing there's a PHQ line …

INTERVIEWER:

Okay.

GP1:

for depression. Erm, so I'd be looking at other psychological explanations and why they maybe feeling pain, why now …

INTERVIEWER:

Uh-huh.

GP1:

looking at the rest of their life, you know they maybe, their life maybe painful …

INTERVIEWER:

Uh-huh.

GP1:

and, erm, they may demonstrate that painful life through something else such as painful diabetic neuropathy.

INTERVIEWER:

Okay.

GP1:

Erm, so I would treat that as I would with any kind of chronic pain.

INTERVIEWER:

Okay and where would your treatment options be from that assessment?

GP1:

Well sometimes with these treatment options, with this sort of approach part of the value is in at least discussing it with the patient and drawing their attention to a possible association with their life …

INTERVIEWER:

Yeah.

GP1:

and their pain …

INTERVIEWER:

Yeah.

GP1:

and sometimes when they realise that then they may stop thinking so much about mediation solutions to their pain and, er, sometimes the pain becomes less of an issue when they can see that association because they become less worried about their pain, they might be just less concerned about it and, therefore …

INTERVIEWER:

Okay.

GP1:

if they're less concerned about it then the pain gets less because so often in, you see people with painful syndrome, but their anxiety about it triggers a lot of thought and rumination …

INTERVIEWER:

Yeah.

GP1:

which makes the pain appear worse which makes the anxiety worse and so on. So if you can help reduce the anxiety that they're, this is a problem, its not necessarily going to get any worse, its not going to be, not necessarily serious, its not a sign of cancer or something disastrous …

INTERVIEWER:

Um.

GP1:

erm, then that can relieve the anxiety which then relieves the pain.

INTERVIEWER:

Yeah.

GP1:

So sometimes just the consultations because it normally takes more than one, erm, talking it through is …

INTERVIEWER:

Is therapeutic …

GP1:

therapeutic.

INTERVIEWER:

… in its own right.

GP1:

Yeah.

INTERVIEWER:

Yeah.

GP1:

Sometimes giving people confidence that they can exercise okay …

INTERVIEWER:

Yeah.

GP1:

that by exercising alright won't do them any harm, in fact it may well do them good both physically and psychologically, so empowering people to live normal lives …

INTERVIEWER:

Uh-huh.

GP1:

and not let the pain take over their lives. So that's a sort of, probably a fairly lightweight GP approach to pain, chronic pain management.

INTERVIEWER:

Lightweight as in sort of psychologically light?

GP1:

Lightweight as in you know I'm not a clinical psychologist …

INTERVIEWER:

Sure.

GP1:

and I'm not sitting down with them for forty five minutes for six weeks …

*Appendix 18 – PDN impact statements*

| | | NVivo code | Survey statement | Type of interference |
|---|---|---|---|---|
| Impact | 1 | sleep disturbance | My sleep is disturbed due to PDN | Rest |
| Impact | 2 | emotional depression | PDN leads me to feel depressed | Mood |
| Impact | 3 | losing mobility | PDN makes walking difficult | Function |
| Impact | 4 | affecting day to day activity | PDN affects my ability to do every day jobs | Function |
| Impact | 5 | numb feet | PDN causes me to have numb feet | Sensory |
| Impact | 6 | what other people think | It bothers me what other people think of me due to the problems I have with PDN | Mood |
| Impact | 7 | becoming socially isolated | I have become more socially isolated due to PDN | Social |
| Impact | 8 | can't sit for too long | PDN stops me from sitting comfortably | Rest |
| Impact | 9 | emotional frustration | PDN leads me to get frustrated | Mood |
| Impact | 10 | PDN difficult to cope with | I don't cope well with PDN | Coping |
| Impact | 11 | a hidden problem no-one else sees | It bothers me that other people can't see I have this problem | Mood |
| Impact | 12 | worries for the future | I am worried that my PDN will get worse in the future | Mood |
| Impact | 13 | affect on partner | My PDN has an affect on my partner | Social |
| Impact | 14 | affecting all aspects of life | PDN affects a wide range of activities that I want to do | Function |
| Impact | 15 | emotional anger | PDN leads me to feel angry | Mood |
| Impact | 16 | keeping it to myself | I keep my problem with PDN away from my close family | Mood |
| Impact | 17 | life pre-PDN | I am not the person I was before I developed PDN | Mood |
| Impact | 18 | regular foot checks | I have to check my feet regularly for possible injury | Function |
| Impact | 19 | affecting concentration | PDN affects my ability to concentrate | Social |
| Impact | 20 | losing balance | I have to be careful walking due to my balance | Function |
| Impact | 21 | not able to do my work | I have difficulty doing my job due to PDN | Employment |
| Impact | 22 | Stepping back from physical activity | I have reduced my physical activity due to PDN | Function |
| Impact | 23 | struggling with social life | PDN affects my social life | Social |
| Impact | 24 | suicide | I have contemplated suicide due to my PDN | Mood |
| Impact | 25 | why me with PDN | I don’t understand why I have PDN | Mood |
| Impact | 26 | crying with pain | PDN hurts so much it brings tears to my eyes | Sensory |
| Impact | 27 | emotional worry | PDN leads me to worry more than I would if I didn’t have it | Mood |
| Impact | 28 | had to stop driving | PDN makes me think about driving carefully | Function |
| Impact | 29 | loss of intimacy | PDN affects my intimate relationships with a partner | Social |
| Impact | 30 | affect on family | My PDN affects my close family | Social |
| Impact | 31 | affecting memory | PDN affects my memory | Function |
| Impact | 32 | can't face food | PDN affects my appetite for food | Function |
| Impact | 33 | fallen over | PDN and balance problems lead me to fall over | Function |
| Impact | 34 | loss of independence | PDN stops me being as independent as I expect to be | Social |
| Impact | 35 | problem with footwear | PDN makes it difficult to buy shoes that are comfortable | Function |
| Impact | 36 | restless legs | PDN gives me a sense of restless legs | Sensory |
| Impact | 37 | skin sensitivity | My skin is sensitive to the lightest touch | Sensory |
| Impact | 38 | am pain not been moving | PDN affects me as soon as I put my foot to the ground in the morning | Sensory |

| | | NVivo code | Survey statement | Type of interference |
|---|---|---|---|---|
| Impact | 39 | feet look normal | My feet look normal but I have this severe pain | Sensory |
| Impact | 40 | headaches | PDN can lead me to have headaches | Sensory |
| Impact | 41 | holidays affected | PDN affects our family holidays | Social |
| Impact | 42 | narrowing down life | My life had become more restricted due to PDN | Function |
| Impact | 43 | not going out | I don't go out as much because of PDN | Social |
| Impact | 44 | struggle to get up for work | I struggle to get up for work due to the PDN | Employment |
| Impact | 45 | worries about money | I worry how our money will be affected because of PDN | Mood |
| Impact | 46 | worry about fitness | I worry about keeping my physical fitness due to PDN | Mood |
| Impact | 47 | be on my own | When PDN flares up I just want to be on my own | Social |
| Impact | 48 | become agoraphobic | PDN makes me worried about going out of the house | Function |
| Impact | 49 | considering others | I always have to think about the needs of other people | Mood |
| Impact | 50 | embarrassed emotion | PDN makes me feel embarrassed | Mood |
| Impact | 51 | getting breathless | I get more breathless than before I had PDN | Function |
| Impact | 52 | getting cramp | I get cramp more frequently than before I has PDN | Sensory |
| Impact | 53 | loss of confidence | I have lost confidence to be myself due to PDN | Function |
| Impact | 54 | no quality of life | My overall quality of life is really affected by PDN | Mood |
| Impact | 55 | pain makes me mean | When PDN flares up I can be less tolerant to those around me | Mood |
| Impact | 56 | self image | My self-image has changed due to PDN | Mood |
| Impact | 57 | stopped dancing | PDN has stopped me going dancing | Function |
| Impact | 58 | extra split of social impact | I keep my problems with PDN away from my wider social network | Social |

*Appendix 19 – Internet survey PIS*

**Research Study Title: An Internet survey investigating the impact of Painful Diabetic Neuropathy (PDN) and patient treatment priorities.**

You are being invited to take part in a study. Before you decide if you want to take part, it is important for you to understand why the study is being done and what it will involve. Please take the time to read the following information carefully. Talk to others about the study if you wish.

Ask us by e-mail if there is anything that is not clear, or if you would like more information. There is an e-mail address at the bottom of this information. Take time to decide whether or not you wish to take part.

**What is the purpose of the study?**

This study is part of a research programme, aiming to improve ways of managing painful diabetic neuropathy (PDN).

This study involves an Internet survey completed by people who experience PDN.

This study aims to find out 1) more about the impact of PDN on an individual's life and 2) what priorities people have for managing the impacts of their PDN.

**Do I have to take part?**

No, it is up to you to decide if you want to take part. We will not contact you directly if you decide not to take part.

**What will the research involve?**

We are asking people that agree to take part to complete an Internet survey. The survey will take about 20 minutes to complete. After you have finished the survey, you will have completed our study and you do not have to do anything else.

The survey involves a range of questions:

- There are brief questions about you and your history of diabetes and PDN.
- There are questions about coping with on-going pain.

These questions are followed by 58 brief statements about the impact that PDN has on people's lives. These statements come from an interview study we conducted with people who experience PDN and reflect the personal, social and mood impacts that they reported.

- You will be asked to identify which of these impacts you experience and, if relevant, how much that impact affects your quality of life.
- You will then be asked to choose up to 10 impacts and put these in the order of priority that you would most like help to manage them better.
- Finally, you will be asked if you have sought help for PDN from any health professional.

**What are the risks and benefits of taking part?**

There are no specific risks to participating in this research.

There are no immediate direct benefits to participating. We hope this research will help develop potential management strategies for PDN in the future that are matched to the priorities of people with the condition.

**What happens when the research study stops?**

We will analyse the data and publish a full report in the academic literature so that other researchers, as well as health care professionals can use the findings. A summary report will also be made available via the Diabetes UK website and Internet forums. The University of the West of England (UWE) will keep the data for 9 years and then it will be destroyed.

**Will my taking part in the study be kept confidential?**
Yes, the survey is completely anonymous. The webpage does not record any hidden information about your location when completing the survey (computer or IP address). The personal information you give in the survey cannot be linked to you personally. All electronic files will be stored on secure password protected servers at UWE Bristol. UK data protection laws protect the security of this data.

**What will happen if I don't want to carry on with the study?**
You may withdraw at any time by exiting the survey webpage. Once you complete the survey, it will not be possible to remove your data, as we will not know which data belongs to you.

**Who is organising the study?**

This study is organised by the University of the West of England, the Royal United Hospital (Bath), and the University Hospitals Bristol NHS Foundation Trust.

This study forms part of a PhD research project at UWE.

The UWE Health and Applied Sciences ethics committee has reviewed and approved this study.

**Access to the survey website**

You can access this survey using this link: Impact of PDN survey

**Further information on painful neuropathy**

If you need further information about any symptoms you experience, please speak to your GP or practice nurse. Other sources of information include the Diabetes UK https://www.diabetes.org.uk and NHS Choices websites http://www.nhs.uk/pages/home.aspx.

**Chief Investigator:**

Ben Davies, MSc, MCSP, PhD candidate.

**PhD supervisory team:**

Professor Candy McCabe, UWE, Royal United Hospital, Bath.

Dr Fiona Cramp, UWE.

Dr Jeremy Gauntlett-Gilbert, Royal United Hospital, Bath.

Professor David Wynick, UHBristol.

*Appendix 20 – Internet survey UWE Ethics approval*

**Faculty of Health & Applied Sciences**
**Glenside Campus**
**Blackberry Hill**
**Stapleton**
**Bristol BS16 1DD**

**Tel: 0117 328 1170**

UWE REC REF No: HAS/15/11/038

3rd December 2015

Ben Davies

Dear Ben

**Application title: An Internet survey investigating the impact of Painful Diabetic Neuropathy (PDN) and patient treatment priorities**

Your ethics application was considered by the Faculty Research Ethics Committee and, based on the information provided, has been given ethical approval to proceed with the following conditions:

1. Although the survey is completely anonymous and the information sheet outlines very clearly the data protection and withdrawal processes, it is important to have a statement for consent before the participant is allowed to move on to the next section and complete the survey. This might have been already planned but it was not clear to me from reading the application. Consent form can be ticked / approved anonymously.
2. Also I am not sure if this will be provided along with the outline of the study, but please provide a list of support /information services that participants can access easily on the information sheet or any documentation which will be used to advertise the study.

If these conditions include providing further information please do not proceed with your research until you have full approval from the committee. You must notify the committee in advance if you wish to make any significant amendments to the original application using the amendment form at http://www1.uwe.ac.uk/research/researchethics/applyingforapproval.aspx.

Please note that any information sheets and consent forms should have the UWE logo. Further guidance is available on the web: http://www1.uwe.ac.uk/aboutus/departmentsandservices/professionalservices/marketingandcommunications/resources.aspx

The following standard conditions also apply to all research given ethical approval by a UWE Research Ethics Committee:

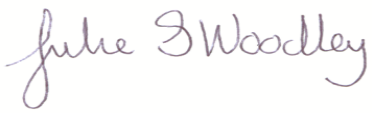
1. You must notify the relevant UWE Research Ethics Committee in advance if you wish to make significant amendments to the original application: these include any changes to the study protocol which have an ethical dimension. Please note that any changes approved by an external research ethics committee must also be communicated to the relevant UWE committee.
2. You must notify the University Research Ethics Committee if you terminate your research before completion;
3. You must notify the University Research Ethics Committee if there are any serious events or developments in the research that have an ethical dimension.

Please note: The UREC is required to monitor and audit the ethical conduct of research involving human participants, data and tissue conducted by academic staff, students and researchers. Your project may be selected for audit from the research projects submitted to and approved by the UREC and its committees.

Please remember to populate the HAS Research Governance Record with your ethics outcome.

We wish you well with your research.

Yours sincerely



Dr Julie Woodley
Chair
Faculty Research Ethics Committee

c.c *Candy McCabe*

*Appendix 21 – Internet pilot survey responses*

| Internet survey ID number | pilot completed ? | reminder sent? 25/1/16 | time to complete (mins) | Comments |
|---|---|---|---|---|
| 1 | | yes | | |
| 2 | | no | | |
| 3 | | yes | | |
| 4 | | yes | | |
| 5 | | yes | | |
| 6 | | yes | | |
| 7 | yes | yes | 26 | |
| 8 | | yes | | |
| 9 | yes | | 33 | At the time my PD was at its worst I received help with hand grips being fitted near steps and in the bath and shower. Also near the toilet. These gave me confidence. When my symptoms were at their worst I could have screamed with the pain, but I received a lot of help from the Pain Management team, and gradually managed over time to reduce the drugs being taken. They also explained my symptoms, which helped me to adjust. |
| 10 | | yes | | |
| 11 | | yes | | |
| 12 | yes | | 43 | Your survey is dedicated to PDN and is well put together. Easy to read and understand. I may have missed it but I think a section on understanding what the cause of PDN and explanation of the effects on the feet and legs. There are other 'syndromes' that produce neuropathic pain, numbness etc., which mimic those caused by diabetes. Perhaps a short question or two surrounding those 'syndromes' Feel free to e-mail if you would like clarification |
| 13 | | yes | 35 | |
| 14 | yes | | 38 | It isn`t easy to "drag" up to 10 statements across |
| 15 | | yes | | |
| 16 | | yes | | |
| 17 | | yes | | |
| 18 | | yes | | |
| 19 | yes | | 32 | The large number of questions on page 7 is still overwhelming. I personally found this section the most difficult to answer |
| 20 | | yes | | |
| 21 | | yes | | |
| 22 | | yes | 23 | |
| 23 | | yes | 9hours | The link you gave me by e-mail enabled easy access to the web-site .I did wonder whether my difficulty was due to having changed to Windows 8?I tried numerous times to get through on my own and had almost given up. If other people experience the same it might be suggest an unwillingness to take part whereas the truth is they did try but couldn't get through. |
| | | **Average** | **32 mins** | |

*Appendix 22 – PDN impacts based on experience*

| | | **Impact statement** | **n=** | % not exp'd (Likert 0) | % Exp'd (Likert 1-4) |
|---|---|---|---|---|---|
| Impact | 18 | I have to check my feet regularly for possible injury | 58 | 5.2 | 94.8 |
| Impact | 12 | I am worried that my PDN will get worse in the future | 61 | 6.6 | 93.4 |
| Impact | 1 | My sleep is disturbed due to PDN | 61 | 8.2 | 91.8 |
| Impact | 5 | PDN causes me to have numb feet | 60 | 8.3 | 91.7 |
| Impact | 9 | PDN leads me to get frustrated | 58 | 10.3 | 89.7 |
| Impact | 40 | My feet look normal but I have this severe pain | 62 | 11.3 | 88.7 |
| Impact | 19 | PDN affects my ability to concentrate | 60 | 13.3 | 86.7 |
| Impact | 37 | PDN gives me a sense of restless legs | 60 | 15.0 | 85.0 |
| Impact | 55 | When PDN flares up I can be less tolerant to those around me | 58 | 15.5 | 84.5 |
| Impact | 3 | PDN makes walking difficult | 61 | 16.4 | 83.6 |
| Impact | 8 | PDN stops me from sitting comfortably | 59 | 16.9 | 83.1 |
| Impact | 27 | PDN leads me to worry more than I would if I didn't have it | 62 | 17.7 | 82.3 |
| Impact | 47 | I worry about keeping my physical fitness due to PDN | 58 | 19.0 | 81.0 |
| Impact | 20 | I have to be careful walking due to my balance | 61 | 19.7 | 80.3 |
| Impact | 53 | I have lost confidence to be myself due to PDN | 61 | 19.7 | 80.3 |
| Impact | 14 | PDN affects a wide range of activities that I want to do | 60 | 20.0 | 80.0 |
| Impact | 43 | My life had become more restricted due to PDN | 60 | 20.0 | 80.0 |
| Impact | 4 | PDN affects my ability to do every day jobs | 58 | 20.7 | 79.3 |
| Impact | 36 | PDN makes it difficult to buy shoes that are comfortable | 61 | 21.3 | 78.7 |
| Impact | 22 | I have reduced my physical activity due to PDN | 60 | 21.7 | 78.3 |
| Impact | 56 | My self-image has changed due to PDN | 60 | 21.7 | 78.3 |
| Impact | 39 | PDN affects me as soon as I put my foot to the ground in the morning | 60 | 23.3 | 76.7 |
| Impact | 48 | When PDN flares up I just want to be on my own | 59 | 23.7 | 76.3 |
| Impact | 17 | I am not the person I was before I developed PDN | 60 | 25.0 | 75.0 |
| Impact | 23 | PDN affects my social life | 60 | 25.0 | 75.0 |
| Impact | 2 | PDN leads me to feel depressed | 59 | 25.4 | 74.6 |
| Impact | 15 | PDN leads me to feel angry | 60 | 26.7 | 73.3 |
| Impact | 26 | PDN hurts so much it brings tears to my eyes | 60 | 26.7 | 73.3 |
| Impact | 10 | I don't cope well with PDN | 59 | 27.1 | 72.9 |
| Impact | 57 | PDN has stopped me going dancing | 58 | 29.3 | 70.7 |
| Impact | 16 | I keep my problem with PDN away from my close family | 60 | 31.7 | 68.3 |
| Impact | 38 | My skin is sensitive to the lightest touch | 59 | 32.2 | 67.8 |
| Impact | 42 | PDN affects our family holidays | 58 | 34.5 | 65.5 |

| | | **Impact statement** | **n=** | % not exp'd (Likert 0) | % Exp'd (Likert 1-4) |
|---|---|---|---|---|---|
| Impact | 33 | PDN and balance problems lead me to fall over | 60 | 35.0 | 65.0 |
| Impact | 35 | PDN stops me being as independent as I expect to be | 60 | 35.0 | 65.0 |
| Impact | 44 | I don't go out as much because of PDN | 60 | 35.0 | 65.0 |
| Impact | 54 | My overall quality of life is really affected by PDN | 57 | 35.1 | 64.9 |
| Impact | 11 | It bothers me that other people can't see I have this problem | 59 | 35.6 | 64.4 |
| Impact | 58 | I keep my problems with PDN away from my wider social network | 59 | 35.6 | 64.4 |
| Impact | 7 | I have become more socially isolated due to PDN | 60 | 38.3 | 61.7 |
| Impact | 25 | I don't understand why I have PDN | 59 | 39.0 | 61.0 |
| Impact | 50 | I always have to think about the needs of other people | 59 | 39.0 | 61.0 |
| Impact | 13 | My PDN has an affect on my partner | 59 | 40.7 | 59.3 |
| Impact | 21 | I have difficulty doing my job due to PDN | 59 | 40.7 | 59.3 |
| Impact | 29 | PDN affects my intimate relationships with a partner | 59 | 40.7 | 59.3 |
| Impact | 28 | PDN makes me think about driving carefully | 58 | 41.4 | 58.6 |
| Impact | 45 | I struggle to get up for work due to the PDN | 58 | 43.1 | 56.9 |
| Impact | 32 | PDN affects my appetite for food | 60 | 43.3 | 56.7 |
| Impact | 49 | PDN makes me worried about going out of the house | 59 | 44.1 | 55.9 |
| Impact | 50 | PDN makes me feel embarrassed | 56 | 44.6 | 55.4 |
| Impact | 30 | My PDN affects my close family | 58 | 44.8 | 55.2 |
| Impact | 6 | It bothers me what other people think of me due to the problems I have with PDN | 60 | 45.0 | 55.0 |
| Impact | 46 | I worry how our money will be affected because of PDN | 59 | 45.8 | 54.2 |
| Impact | 51 | I get more breathless than before I had PDN | 56 | 48.2 | 51.8 |
| Impact | 52 | I get cramp more frequently than before I has PDN | 58 | 50.0 | 50.0 |
| Impact | 31 | PDN affects my memory | 59 | 50.8 | 49.2 |
| Impact | 41 | PDN can lead me to have headaches | 58 | 53.4 | 46.6 |
| Impact | 24 | I have contemplated suicide due to my PDN | 58 | 70.7 | 29.3 |

*Appendix 23 – PDN impacts based on severity*

| | | **Impact statement** | n= for Likert 1-4 | **% 3 or 4/4** | **% 1 or 2/4** |
|---|---|---|---|---|---|
| Impact | 12 | I am worried that my PDN will get worse in the future | 57 | 84 | 16 |
| Impact | 11 | It bothers me that other people can't see I have this problem | 38 | 76 | 24 |
| Impact | 52 | I get cramp more frequently than before I has PDN | 29 | 76 | 24 |
| Impact | 1 | My sleep is disturbed due to PDN | 56 | 75 | 25 |
| Impact | 9 | PDN leads me to get frustrated | 52 | 75 | 25 |
| Impact | 14 | PDN affects a wide range of activities that I want to do | 48 | 75 | 25 |
| Impact | 5 | PDN causes me to have numb feet | 55 | 75 | 25 |
| Impact | 40 | PDN can lead me to have headaches | 55 | 75 | 25 |
| Impact | 22 | I have reduced my physical activity due to PDN | 47 | 74 | 26 |
| Impact | 23 | PDN affects my social life | 31 | 74 | 26 |
| Impact | 53 | I have lost confidence to be myself due to PDN | 49 | 73 | 27 |
| Impact | 36 | PDN gives me a sense of restless legs | 48 | 73 | 27 |
| Impact | 47 | When PDN flares up I just want to be on my own | 47 | 72 | 28 |
| Impact | 21 | I have difficulty doing my job due to PDN | 35 | 71 | 29 |
| Impact | 18 | I have to check my feet regularly for possible injury | 55 | 71 | 29 |
| Impact | 43 | I don't go out as much because of PDN | 48 | 71 | 29 |
| Impact | 57 | PDN has stopped me going dancing | 41 | 71 | 29 |
| Impact | 56 | My self-image has changed due to PDN | 47 | 70 | 30 |
| Impact | 10 | I don't cope well with PDN | 43 | 70 | 30 |
| Impact | 55 | When PDN flares up I can be less tolerant to those around me | 49 | 69 | 31 |
| Impact | 46 | I worry about keeping my physical fitness due to PDN | 32 | 69 | 31 |
| Impact | 42 | My life had become more restricted due to PDN | 38 | 68 | 32 |
| Impact | 2 | PDN leads me to feel depressed | 44 | 68 | 32 |
| Impact | 7 | I have become more socially isolated due to PDN | 37 | 68 | 32 |
| Impact | 38 | PDN affects me as soon as I put my foot to the ground in the morning | 40 | 68 | 33 |
| Impact | 3 | PDN makes walking difficult | 51 | 67 | 33 |
| Impact | 23 | I have contemplated suicide due to my PDN | 45 | 67 | 33 |
| Impact | 27 | PDN makes me think about driving carefully | 51 | 67 | 33 |
| Impact | 35 | PDN makes it difficult to buy shoes that are comfortable | 39 | 67 | 33 |
| Impact | 44 | I struggle to get up for work due to the PDN | 39 | 67 | 33 |
| Impact | 15 | PDN leads me to feel angry | 44 | 66 | 34 |
| Impact | 26 | PDN leads me to worry more than I would if I didn’t have it | 44 | 66 | 34 |
| Impact | 30 | PDN affects my memory | 32 | 66 | 34 |

| | | **Impact statement** | n= for Likert 1-4 | **% 3 or 4/4** | **% 1 or 2/4** |
|---|---|---|---|---|---|
| Impact | 48 | PDN makes me worried about going out of the house | 45 | 64 | 36 |
| Impact | 6 | It bothers me what other people think of me due to the problems I have with PDN | 33 | 64 | 36 |
| Impact | 20 | I have to be careful walking due to my balance | 49 | 63 | 37 |
| Impact | 58 | I keep my problems with PDN away from my woder social network | 38 | 63 | 37 |
| Impact | 4 | PDN affects my ability to do every day jobs | 46 | 63 | 37 |
| Impact | 39 | My feet look normal but I have this severe pain | 46 | 63 | 37 |
| Impact | 13 | My PDN has an affect on my partner | 35 | 63 | 37 |
| Impact | 29 | My PDN affects my close family | 35 | 63 | 37 |
| Impact | 17 | I am not the person I was before I developed PDN | 45 | 62 | 38 |
| Impact | 28 | PDN affects my intimate relationships with a partner | 34 | 62 | 38 |
| Impact | 19 | PDN affects my ability to concentrate | 52 | 62 | 38 |
| Impact | 33 | PDN stops me being as independent as I expect to be | 39 | 62 | 38 |
| Impact | 8 | PDN stops me from sitting comfortably | 49 | 61 | 39 |
| Impact | 16 | I keep my problem with PDN away from my close family | 41 | 61 | 39 |
| Impact | 49 | I always have to think about the needs of other people | 33 | 61 | 39 |
| Impact | 25 | PDN hurts so much it brings tears to my eyes | 36 | 58 | 42 |
| Impact | 37 | My skin is sensitive to the lightest touch | 51 | 57 | 43 |
| Impact | 50 | PDN makes me feel embarrassed | 36 | 56 | 44 |
| Impact | 31 | PDN affects my appetite for food | 29 | 55 | 45 |
| Impact | 51 | I get more breathless than before I had PDN | 29 | 55 | 45 |
| Impact | 45 | I worry how our money will be affected because of PDN | 33 | 55 | 45 |
| Impact | 24 | I don’t understand why I have PDN | 17 | 53 | 47 |
| Impact | 54 | My overall quality of life is really affected by PDN | 37 | 49 | 51 |
| Impact | 41 | PDN affects our family holidays | 27 | 48 | 52 |
| Impact | 32 | PDN and balance problems lead me to fall over | 34 | 47 | 53 |

*Appendix 24 – Free text additions*

| ***Free text addition*** | ***Current or new code*** |
|---|---|
| It doesn't affect my life except when HCPs assume it is Diabetic - I don't believe it is! - so though I have pain when the duvet touches that exact spot on the one big toe, it has no other effect. I thought the numbness in my feet and the loss of balance were caused by hardening of the arteries, I didn't know neuropathy even caused that? | Code: sleep disturbed<br>Code: skin sensitivity<br>Code: numb feet<br>Code: causes of symptoms |
| been admitted to hosp with stomach nerve pain | **New code: autonomic neuropathy** |
| Added to the intermittent claudication, it has exacerbated the already worrying concern for my longevity and QOL | Code: future worries |
| agonizing pins and needles that make me cry | Code: crying with pain |
| It's bloody awful terrible condition | Code: affects all aspects of life |
| Self harming behaviour -not suicidal ideation. Cutting legs and hands and tying things around them to cut off circulation. I am a professional and am required to work long stressful hours. I cannot take the medication I need to knock me out so I am not exausted. I have this year had very high sickness absence. | Code: suicide<br>**New code: self harming behaviour**<br>Code: fatigue with PDN<br>Code: not able to do my work<br>Code: side effects of medication |
| PDM stopped me dancing - but I've recently discovered it helps reduce toe numbness and pain intensity, whereas medication didn't. | Code: stopped dancing<br>Code: feeling better with activity<br>Code: medication not working |
| struggle to use my hands/make a fist/grip things....hands go numb. worst in bed so have to get out of bed to shake my hands standing up then struggle to get back to sleep. | **New code: hand numbness**<br>Code: sleep disturbance<br>Code: getting up in the night |
| In so much pain at times I just cry with the level of pain I am in. Pain so bad at times unable to prepare meals. | Code: crying with pain<br>Code: affecting all aspects of life (or **new code specific to meal preparation)** |
| Do you feel fire in your feet?, I do every night and first thing in the morning. | Code: Templar torture<br>Code: morning pain |
| Mine is cramp in my toes all the time | Code: getting cramps |
| Worry of having to amputate my feet | Code: future worries |
| I have also had toes amputated after a fall | Code: losing balance<br>Code: fallen over |
| fear of going out and not being able to keep walking long enough to get back home | Code: not going out<br>Code: losing mobility<br>Code: losing confidence |

*Appendix 25 – Publications and accepted abstracts*

**Publications**

Davies B., Cramp F., Gauntlett-Gilbert J., Wynick D., McCabe CS. 2015. The role of physical activity and psychological coping strategies in the management of painful diabetic neuropathy – A systematic review of the literature. *Physiotherapy*, 101(4), pp.319–326.

**Accepted abstracts**

**European Pain Federation EFIC – Copenhagen – September 2017.**

04. Pain treatment (conservative)

4.06 Neuropathic pain

Poster Board

AN INTERNET SURVEY EXPLORING THE TREATMENT PRIORITIES OF PEOPLE WITH PAINFUL DIABETIC NEUROPATHY (PDN)

BACKGROUND AND AIMS

PDN is a neuropathic pain condition which has significant impact on patients' quality of life. Analgesia is the main management strategy but recommended medications are often ineffective at controlling pain to manageable severity. This survey aimed to understand the treatment priorities of people with PDN

METHODS

Previous qualitative research produced a set of 58 impacts, related to PDN. An Internet survey was conducted to explore which of these impacts were peoples' priorities for better management strategies. Respondents short-listed 10 impacts, then ordered these by priority for better management. This survey was advertised by DiabetesUK and posted to major patient forums for diabetes.

RESULTS

There were n=107 responses, with n=78 meeting pre-set diagnostic criteria for PDN. The sample were 55% female, 63% had Type 2 diabetes, aged mean 57(SD13) years. Respondents had diabetes for mean 17.8(13.7) years and PDN for mean 7.3(6.3) years. The priorities of subgroups (gender, type of diabetes, high/low pain and whether they had sought help for PDN) were analysed. Sleep disturbance was consistently the top priority amongst subgroups. Physical fitness, walking, numb feet, anxiety and depression were consistently prioritised by at least half the subgroups analysed (see table 1). Impacts describing pain experience were not prioritised by respondents.

CONCLUSIONS

People with PDN may have other priorities than pain reduction. Clinicians need to ensure that advice and treatment are focussed on the patients' impacts of most importance.

**British Pain Society ASM Birmingham 2017 parallel workshop**

| | |
|---|---|
| **Title of Session** | Physiotherapy and Physical Activity Approaches in Persistent Pain |
| **Session Organiser** | Dr Jane Hall, Senior Clinical Research Physiotherapist |
| **Organisers contact details** | CRPS Service, Bath Centre for Pain Services, Royal National Hospital for Rheumatic Diseases, Upper Borough Walls, Bath, BA1 1RL |
| **Session summary** | This session will consider patient and health professional understanding and approaches to physical activity within the context of three long term conditions (Peripheral Diabetic Neuropathy, Osteoarthritis and Complex Regional Pain Syndrome). The safety and effectiveness of regular physical activity and exercise will be considered via patients' concerns of condition exacerbation. A neurocognitive therapeutic model which changes the associations and perception about pain will be described in terms of application in a rehabilitation context. Attendees will gain insight into emerging treatment paradigms and barriers to patient engagement and discussion will stimulate consideration of different perspectives in long-term rehabilitation and physical activity strategies |
| **Speaker 1** | Ben Davies, Clinical Specialist Physiotherapist in Pain Management |
| **Presentation Title** | Considering physical activity for people who have painful diabetic neuropathy. |

**World Congress of Physical Therapy – European Region, Liverpool 2016.**

## Should pain management programmes strategies be part of managing painful diabetic neuropathy (PDN)? (Poster)

Ben Davies[1], Fiona Cramp[1], Jeremy Gauntlett-Gilbert[1,2], Candida McCabe[1,2]

[1] Faculty of Health and Applied Sciences, University of the West of England, Bristol UK.

[2] Royal United Hospital, Bath, UK

**Abstract body**

**Relevance.** Diabetes is increasing in prevalence and globally ranks 14th for its impact on quality adjusted life years. PDN is a distressing and disabling condition occurring in 6-34% of people with diabetes. Despite extensive involvement in managing a wide range of patients with chronic pain, physiotherapists do not routinely manage people with PDN.

**Purpose.** Analgesic medications are the predominant treatment for PDN yet they are often reported as inadequate. Multidisciplinary pain management programme may be beneficial for people with PDN. The key management strategies for these programme are graded physical activity (PA) and psychological coping skills (PsyCS). The objectives of this study were to: (1) interview people with PDN to explore the impact of PDN, management strategies for PDN and perspectives on PA and PsyCS; (2) interview diabetes and pain management clinicians to explore their perspectives on pain management strategies.

**Methods/Analysis.** Semi-structured interviews were conducted with people who experience PDN. Recruitment was through local PDN clinics and a nationwide advert. All participants had PDN and could communicate in English without the need of an interpreter. No other exclusion criteria were applied. Clinicians with appropriate expertise were identified and approached to participate. At least two representatives from key professions were sought. Interviews were conducted face-to-face or by telephone, audio recorded, transcribed and analyzed using Inductive Thematic Analysis. University and NHS Ethics Committees (Frenchay 13/SW/0125) granted ethical approval.

**Results.** Twenty-three people with PDN were interviewed (mean age 62yrs, range 24-86, 12 women, 10 Type 1 diabetes, 22 White British). In total 58 impacts of PDN were identified. A wide range of management techniques had been tried. People were concerned about future health and fitness and wanted advice about PA from professionals, but did not want their pain to be exacerbated. Few people had accessed PsyCS, but those who had, reported benefits. A strong theme developed that psychology played no part in peoples' experiences, and hence PsyCS were not appropriate.

Nineteen clinicians from primary and secondary care were interviewed. Diabetes specialists often felt clinically impotent when analgesic strategies failed. The majority were unaware of, or did not consider referral to PMPs. Podiatrists expressed concern that PA could damage insensate feet.

Pain management specialists suggested that programme were person, not pathology specific and could be adapted for people with PDN.

**Discussions and conclusions.** It may be possible to adapt pain programme to meet the needs of people with PDN. Consideration would need to be given to the multiple co-morbidities and complications that people with PDN experience.

Patient uncertainty regarding the appropriateness of PA and PsyCS would also need to be addressed. The findings from this study need to be explored in a wider population to determine the management priorities of people with PDN.

**Impact and Implications.** PDN is a significant and disabling pain condition, with significant costs. There are differing perspectives from patients and specialist clinicians, whether PA and PsyCS should become part of a broader approach to management of PDN. The findings from this research have informed an internet survey that is currently being carried out to determine patients' priorities for PDN management.

## Health and Applied Sciences postgraduate research conference, UWE 2015.

### How does painful diabetic neuropathy affect peoples' lives, and how might pain management strategies be an acceptable management pathway? (Presentation)

Ben Davies[1], Fiona Cramp[1], Jeremy Gauntlett-Gilbert[1,2], Candida McCabe[1,2]

[1] Faculty of Health and Applied Sciences, University of the West of England, Bristol UK.

[2] Royal United Hospital, Bath, UK

**Abstract body:**

**Background.** Painful diabetic neuropathy (PDN) is a significant complication of diabetes that is associated with: unpredictable pain, difficulty with everyday tasks, sleep disturbance and emotional distress. Existing drug management is only partially successful. Pain management program, consisting of physical rehabilitation and psychological coping skills may have potential in PDN management. Prior to investigating these programme it was important to explore the impact that PDN has on an individual and the acceptability of such program.

**Method.** Semi-structured 1:1 interviews were conducted with people who experience PDN; they were recruited from a national sample. These interviews were analysed using thematic analysis.

**Results.** Interviews were conducted with 23 participants. Some themes reflected the existing knowledge of PDN – the impact PDN has on sleep, walking and employment. Other themes were new – *increasingly on my own, a shrinking world* and *a very personal problem*. Participants had received drug management from the NHS and had experimented with many strategies to try and cope with PDN. Participants were worried about maintaining physical activity for health reasons and were open to advice from a health professional for exercise that would not worsen their PDN. There were mixed opinions about the acceptability of psychologically based coping skills.

**Implications.** The impact of PDN is more multi-faceted than the existing literature suggests. Some of these impacts would appear suitable for management with existing pain management strategies. Further research is required to identify which of these impacts patients would prioritise for management and explore if these priorities match to existing evidenced treatments.

**Physiotherapy UK conference 2014**

**The patient's experience of managing painful diabetic neuropathy (Presentation).**

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**Abstract body**

**Purpose.** People with painful diabetic neuropathy (PDN) are primarily managed with medication with variable outcomes.

This research explored the experiences of people with PDN including impact on daily living, personal management strategies and views relating to multidisciplinary pain management programme strategies.

**Relevance.** A purposive sample was recruited from local secondary care diabetes/podiatry clinics and nationwide recipients of Balance magazine (DiabetesUK). All adults with PDN with conversational level English were eligible. Targeted selection of respondents was used to capture a breadth of demographic variables. Twelve participants (5 male, 4 Type 1, 11 white British, 1 West Indian, mean age 60.7(SD10.7) years, mean diabetes duration 24.4(12.7) years, mean PDN duration 10.6(5.1) years) were interviewed.

**Methods.** Semi-structured interviews were conducted, either face to face or via telephone. Interviews were transcribed verbatim and anonymised.

**Analysis.** Data were analysed using inductive thematic analysis. Expert patient research partners were engaged in the review of themes produced.

**Results.** PDN impacts on all aspects of personal, social and emotional life. Management is nearly entirely pharmacological, only two participants had experienced psychological coping interventions. Participants had tried numerous self-management strategies including relaxation, cannabis and walking on stinging nettles. Participants reported distress due to PDN and the majority were open to pain coping strategies. Some participants were however unable to reconcile psychological processes with pain attributed to nerve damage.

**Conclusions.** Pharmacological management of PDN does not fully address the impact of PDN on daily living. The principles of multi-disciplinary pain management programme appear to be acceptable to a majority of patients and may have the potential to improve coping strategies.

**Implications.** Research is needed to develop and test a PDN specific pain coping programme.

**British Pain Society conference 2014**

**Painful diabetic neuropathy. Patient and clinician perspectives on current management and multidisciplinary pain management strategies. (Poster).**

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**Abstract body:**

**Background**. Painful diabetic neuropathy (PDN) affects 20% of people with diabetes (Daousi *et al.*, 2004). Diabetes is increasing in prevalence, so is the number of people experiencing the burning pain, associated cognitive distress and functional limitations of PDN (Alberti & Zimmet, 2013). PDN is managed primarily with neuropathic pain medications, there is a range of evidenced pharmacological guidance (Spallone, 2012), however analgesic failure is common (Moore *et al.*, 2013) and people remain in pain and distress (Gore *et al.*, 2006). People with PDN are rarely referred to multidisciplinary pain programme where the key approaches are physical and psychological rehabilitation strategies. It is unclear if the design of these programme is appropriate for a purely neuropathic pain problem. A qualitative study was designed to answer the questions: 1) how do patients experience management of PDN and 2) what are the perspectives and attitudes of clinicians and patients to multidisciplinary pain management strategies?

**Methods**. This study used semi-structured interviews with clinicians and patients. Clinicians were purposively sampled from the primary and secondary care multidisciplinary team, who help people to manage diabetes and PDN. Clinicians included Consultants, Primary and Secondary care nurses, Podiatrists, Psychologists and Physiotherapists. Patients with PDN were recruited from secondary care diabetes clinics and a tertiary care PDN clinic. One-to-one interviews were conducted and transcribed verbatim. The data was coded using a Thematic Analysis approach (Braun & Clarke, 2012) and analysis was completed in collaboration with an Expert Patient Research Partner (EPRP). Thematic analysis is a flexible methodology that is appropriate for seeking patterns across a dataset. From these codes, themes were developed that addressed the research questions.

**Results**. Data analysis is ongoing but four early themes are present. 1) Patients' experience of PDN; patients frequently do not associate pain with diabetes and do not raise it with diabetes clinicians. 2) Clinicians considering PDN; clinicians describe not asking about pain, through oversight or because they have limited therapeutic options. 3) Early diagnosis and management of PDN; patients can experience symptoms for years before accessing treatment, they feel passed from pillar to post, they can be recommended inappropriate analgesia (NSAIDs), or appropriate

analgesia (Amitriptyline) without appropriate review. Finally, 4) Access to specialist opinion; clinicians and patients alike describe being at a loss for the next step in a pathway, medication optimisation is not clear, all clinicians describe patients with significant depression and anxiety. All participants consider pain management strategies could be useful. There is uncertainty what form the physical rehabilitation should take and this is the focus of another study.

**Conclusions**. PDN is a significant problem to those that experience it, analgesia helps but has minimal impact on patients's functioning and levels of distress. Clinicians and patients are open to the option of multidimensional rehabilitation. Such rehabilitation is not highlighted in guidance documents or care pathways. Some uncertainty remains over the exact nature of the physical activity indicated for painful neuropathy and this is the focus of another study. The inclusion of multidisciplinary pain management strategies appears appropriate in guidelines for PDN management.

**Bristol Research in practice symposium, 2014**

## Painful diabetic neuropathy: A systematic review of physical activity and psychological coping strategies. (Presentation).

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**Abstract body:**

**Background**. The prevalence of diabetes is rising. Painful diabetic neuropathy (PDN) is a microvascular complication affecting 16-20% of people with diabetes. It is a burning pain that is significantly associated with impairments to mobility, sleep quality, and life capacity. PDN is currently managed with medication but its effectiveness is variable. People with PDN are rarely referred to pain management programme that use physical rehabilitation and psychological coping strategies to maximise quality of life.

**Aim**. To perform a systematic review of literature relating to physical activity and psychological coping strategies for the management of PDN.

**Methods**. A keyword search was applied to ten databases. Studies were included if they used controlled methods to investigate physical activity or psychological coping strategies for the management of pain and/or pain related distress due to PDN. Studies were assessed for bias and critically appraised.

**Results**. Four studies, of variable quality, were identified for inclusion. One non-randomised study investigated Tai Chi and reported improvements in SF36 domains including bodily pain (Ahn and Song, 2012). Three randomised controlled studies investigated psychological interventions. mindfulness meditation was reported to have no effect on pain or quality of life (Teixeira, 2010), although the required sample size was not obtained. Solution focussed therapy was reported to impact on self-reported problems, but these were not necessarily related to pain (Didjurgeit *et al.*, 2002). Finally, a pilot study of cognitive behavioural therapy reported a decline in pain severity and interference in the intervention group (Otis *et al.*, 2013).

**Discussion.** Four studies have investigated the impact of physical activity or psychological strategies on pain and distress experienced by people with PDN. Clear conclusions of treatment efficacy cannot be drawn from the literature and it is not currently possible to make recommendations for practice. Further high quality studies using clearly defined physical and/or psychological rehabilitation strategies and measuring subjective pain and related distress outcomes are required.

**Allied Health Professions conference, Bristol, 2014.**

## Clinician and patient perspectives on multidisciplinary rehabilitation for painful diabetic neuropathy (PDN). (Commended poster).

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**Abstract body:**

**Aim**: A qualitative study was designed to answer the questions: 1) how do patients experience management of PDN and 2) what are the perspectives of clinicians and patients to multidisciplinary pain management strategies?

**Method**: Semi-structured interviews were conducted with clinicians and patients. Clinicians were purposively sampled from the primary and secondary care multidisciplinary teams, who manage diabetes and PDN. Patients with PDN were recruited from secondary care diabetes and PDN clinics. One-to-one interviews were conducted and transcribed verbatim. Data was coded and analysed using a Thematic Analysis approach (Braun & Clarke, 2012) in collaboration with an Expert Patient Research Partner (EPRP). Thematic analysis is a flexible methodology that is appropriate for seeking patterns across a dataset. From these codes, themes were developed that addressed the research question.

**Results**: Analysis is ongoing but four early themes are present. 1) Patients' experience of PDN; patients may not associate pain with diabetes and do not raise it with clinicians. 2) Clinicians considering PDN; clinicians do not consistently inquire about pain, through oversight or due to limited therapeutic options. 3) Early diagnosis and management of PDN; patients experience symptoms for significant duration before accessing treatment, they feel bounced between clinics, they may be recommended inappropriate analgesia (NSAIDs), or appropriate analgesia (Amitriptyline) without appropriate review. Finally, 4) Access to specialist opinion; clinicians describe patients in pain with cognitive distress where analgesic options have failed. All participants consider pain management strategies could be beneficial.

**Conclusion**: PDN is a significant personal and medical problem. Analgesia is the mainstay of treatment but can be ineffectual. Clinicians and patients are open to the option of multidimensional rehabilitation. Such rehabilitation is not highlighted in guidance documents or care pathways. Uncertainty remains over the nature of the physical activity indicated for painful neuropathy and this is the focus of another study. The inclusion of multidisciplinary pain management strategies warrants further research.