Psychological stress and musculoskeletal pain: the moderating effect of childhood and adulthood trauma

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Abstract

The aetiology of widespread musculoskeletal pain is complex. Psychological stress is a robust predictor of symptom onset and persistence but not everyone who experiences stress goes on to develop widespread pain. The aim of the studies presented in this thesis was to ascertain whether individuals with a history of trauma have an increased susceptibility to widespread pain when they experience psychological stress; to identify psychosocial mediators of the stress pain relationship, and ascertain whether these mediators differ, i.e. are moderated by, the experience of prior trauma and by sex.

The trauma diathesis stress model of widespread pain, developed by the author, was assessed using structural equation modelling on data collected by two population-based prospective studies. In the General Practice Symptom Survey (GPSS), 1,443 adults aged 25–65 years provided data on the number of pain sites, psychological stress and childhood abuse. In the North Staffordshire Osteoarthritis Project (NorStOP), 6,678 adults aged 50–90 years provided data on the number of pain sites and psychological stress, whilst the occurrence of surgeries, fractures, RTAs and burns was obtained from their medical records.

Higher levels of psychological stress were associated with a higher number of pain sites. The stress pain relationship was moderated by childhood abuse but not by adult physical trauma. The relationship between stress and pain was mediated by attachment style (GPSS) and by social support (NorStOP).

This research explored the moderators (in whom) and mediators (how) of the stress pain relationship. Childhood abuse was identified as a susceptibility factor and adult attachment style and social support as the processes by which stress leads to pain. These findings have implications for both primary and secondary prevention; suggesting that a stratified treatment approach may be most appropriate.

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List of abbreviations

ACR	American College of Rheumatology
ACTH	Adrenocorticotropic hormone
AIC	Akaike Information Criterion
AMOS	Analysis of Moment Structures
AVP	Arginine vasopressin
BSNI	Berkman-Syme Social Network Index
CBT	Cognitive Behavioural Therapy
CI	Confidence Interval
CPSAQ	Childhood Physical and Sexual Abuse Questionnaire
CRF	Corticotrophin-releasing factor
CWP	Chronic widespread pain
CWP-M	Chronic widespread pain – Manchester criteria
DBT	Dialectical Behaviour Therapy
DES-T	Dissociative Experiences Scale - Taxon
DfE	Department for Education
DSM	Diagnostic and Statistical Manual
EMDR	Eye Movement Desensitisation and Reprocessing
FM	Fibromyalgia
GABA	Gamma-aminobutyric acid
GP	General Practitioner
GPSS	General Practice Symptom Survey
HADS	Hospital Anxiety and Depression Scale
HPA	Hypothalamic-pituitary-adrenal (HPA) axis
IASP	International Association for the Study of Pain
IPQ-R	Illness Perception Questionnaire - Revised
LFESSQ	London Fibromyalgia Epidemiology Study Screening Questionnaire
LTE	Life Threatening Events scale
MAR	Missing data - Missing completely at random
MCAR	Missing data - Missing at random
MGA	Multiple Group Analysis
MRC	Medical Research Council
NHS	National Health Service
NMAR	Missing data - Not missing at random
NorStOP	North Staffordshire Osteoarthritis Project
NSPCC	National Society for the Prevention of Cruelty to Children
ONS	Office of National Statistics
OR	Odds ratio
PBI	Parental Bonding Instrument
PTSD	Post-Traumatic Stress Disorder
RMSEA	Root Mean Square Error of Approximation
RMR	Root Mean Square Residual
RQ	Relationship Questionnaire
RR	Relative risk
RRR	Relative risk ratio
RTA	Road Traffic Accident
SAS	Somatosensory Amplification Scale
SPS	Sleep Problem Scale
SPSS	Statistics Package for Social Sciences
SRMR	Standardised Root Mean Square Residual
SSI	Somatic Symptom Inventory
WI	Whitely Index
WP	Widespread pain

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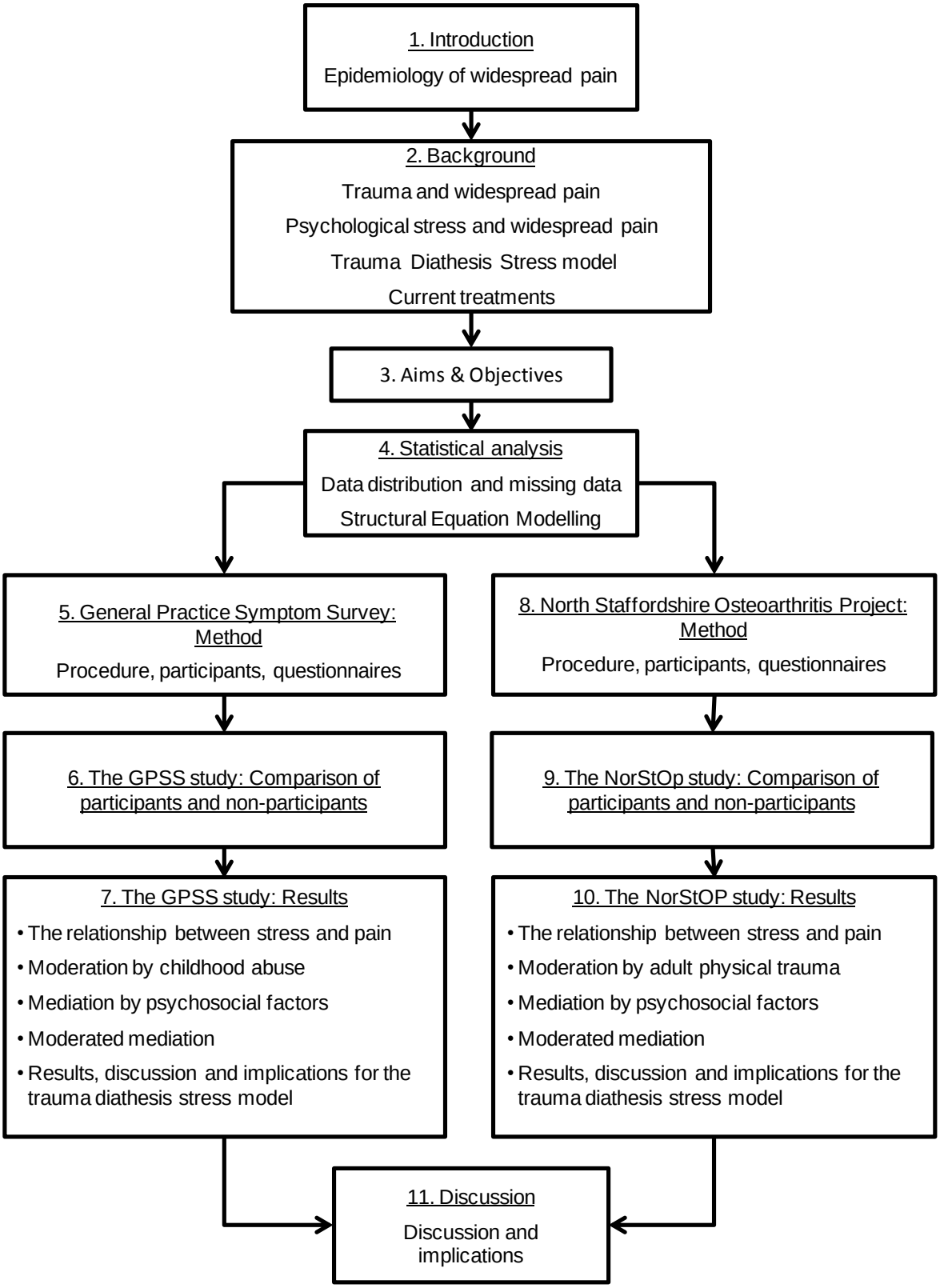
I am not what happened to me.

I am what I choose to become.

Carl Jung

Overview of thesis



Chapter 1 Introduction: Widespread pain

1.1 Chapter overview

The aim of this thesis was to ascertain whether individuals with a history of trauma have an increased susceptibility to widespread musculoskeletal pain when they experience psychological stress. This chapter outlines the epidemiology of widespread musculoskeletal pain within the current literature. As widespread musculoskeletal pain has typically been considered as a chronic, i.e. a long term pain condition, the first section of this chapter examines the distinction between acute and chronic pain. The second section describes the three main ways in which widespread musculoskeletal pain has been conceptualised and assessed. Within each description the prevalence of widespread musculoskeletal pain is evaluated. The final section of this chapter presents a review of the research that demonstrates that widespread musculoskeletal pain is disabling and costly, and represents a significant health concern.

1.2 Acute and chronic pain

> *"Acute pain is the normal, predicted physiological response to a noxious chemical, thermal or mechanical stimulus and typically is associated with invasive procedures, trauma and disease. It is generally time-limited"*
>
> (Federation of States Medical Boards of the United States, 2004, pg5)

Acute pain can be extremely useful, by alerting an individual to the presence of injury, infection or disease. Acute pain forces action to be taken by the individual, such as seeking medical aid or taking rest for recuperation. Acute pain can thus be used to identify and address underlying pathology. In this way, pain can be classed as a symptom (Croft et al, 2010). However, the pain experienced by an individual does not necessarily always correspond to underlying pathology (Kongsted et al, 2008). For example, no clear organic pathology is found in 80-95% of back pain sufferers (Traue et al, 2010; Wassenaar et al, 2007). This subjective variability in the experience of pain suggests that

factors other than physical pathology are involved (Gatchel et al, 2007). Indeed, pain is defined as

> *"an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"*
>
> (International Association for the Study of Pain [IASP] 2011).

As with perception from other senses like vision, pain is a complex balance between bottom-up sensory processing and top down cognitive interpretation. Bottom up processing involves signals from noxious stimuli travelling to the brain via the spinal cord. This provides information relating to the intensity and location of pain. At the same time, inhibitory and facilitatory signals sent from the brain modulate the subsequent nociceptive activity. Psychological and social factors thus influence the subjective experience of pain (Jones et al, 2010; Eysenck & Keane, 1995). For example, pain tolerance can be increased by distraction (Wright & Raudenbush, 2010) and the intensity of pain can be increased by focused attention (Villemure et al, 2002). The placebo effect, which involves a combination of expectation and classical conditioning (Klinger et al, 2007) also provides evidence of top-down processing. For example, negative expectation has been shown to negate the analgesic effects of the opioid remifentanil, whilst positive expectations doubled its effects (Bingel et al, 2011). Pain perception is thus a complex process, consisting of sensory-discriminative, motivational-affective and evaluative dimensions (Melzack, 1999). The perception of sensory inputs from cutaneous, visceral and other somatic receptors is influenced by mood and cognitive factors (Millan, 2002) and the meaning of pain to the individual at that specific point in time (Morris, 1999).

This dissociation between pathology and the subjective experience of pain becomes even more apparent when we consider chronic pain. The IASP (2003) define chronic pain as

> *"pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months)".*
>
> (Harstall & Ospona, 2003, pg1)

Chronic pain can become independent of any precipitating injury, creating its own pathology with its own symptoms, and can thus be classed as a condition in its own right (Siddall & Cousins, 2004). In support of this viewpoint, evidence for functional, anatomical and neurochemical changes in individuals with chronic pain has been suggested by neuroimaging studies (Tracey & Bushnell, 2009). Different patterns of activation have been found in the brain regions associated with acute and chronic pain. A shift from the sensory-discriminative lateral areas to the motivational-affective medial areas suggests that the cognitive and emotional elements of pain perception become more salient in chronic pain rather than the actual intensity of the noxious stimulus (Tracey & Bushnell, 2009). A reduction in grey matter volume has also been found in areas relating to nociceptive processing in chronic pain patients when compared to healthy controls (Rodriguez-Raecke et al, 2009). This is a promising and growing area of research with a significant future aligned with the advancement of technology. However, at present the results should be treated with caution (Ekstrom, 2010); studies often use only a small number of participants and the findings are not always easy to interpret due to the amount of data obtained (Lindquist, 2008; Tracey, 2008).

By its very definition "pain without apparent biological value that has persisted beyond the normal tissue healing time" chronic pain is no longer linked to initiating injury, infection or disease, if one had been identified at all. The likelihood of an individual developing chronic pain appears less dependent on any precipitating cause of acute pain and more dependent upon the individual's "environmental" context, including psychological and social factors (Siddall & Cousins, 2004, pg514). Individuals with chronic pain, and especially with pain that is widespread, experience a number of other physical and psychological problems, as discussed below, which could be classed as symptoms of their pain. Pain thus

> *"has a dual nature. It is both a classic manifestation of, and signpost to, diagnosis in many different diseases and, at the same time, a symptom in its own right needing relief and attention"* (Croft et al, 2010, pg3).

The prevalence of chronic pain in developed countries is high. Estimates range from 24% to 55%, with 12% of individuals experiencing chronic pain that is disabling (Croft, 2010). In the UK, over 4.6 million visits to general practitioners are related to chronic pain (Besley, 2002). Chronic pain can therefore be seen as a "public health problem of epidemic proportions" (Sessle, 2012, pg1).

This section has demonstrated that there is a difference between acute and chronic pain. Acute pain is an adaptive response to a threat to the integrity of the organism, whilst the purpose of persistent or chronic pain is less obvious. The distinction between acute and chronic pain is not limited to duration. Chronic pain has symptoms of its own and can be classed as a condition it is own right. Musculoskeletal pain, the most predominant form of chronic pain, is examined more fully below.

1.3 Musculoskeletal pain

Approximately 90% of chronic pain sufferers report pain in the musculoskeletal system (Andersson et al, 1999). Pain attributed to the musculoskeletal system arises from the bones, joints, muscles, tendons and ligaments (Arendt-Nielson et al, 2011). Musculoskeletal pain conditions include regional pain at a single site; painful disorders such as osteoarthritis and rheumatoid arthritis; and also widespread pain disorders, including fibromyalgia. Together these conditions affect approximately 20% of adults (Woolf & Pfleger, 2003), and account for 20% of all primary care consultations in the UK (Jordan et al, 2007). Studies report point prevalence rates of approximately 17%, 19% and 25% for shoulder, knee and low back pain respectively (Carnes et al, 2007). Prevalence figures vary due to differences in definitions and the populations tested, as described below. However, it is clear that the reporting of musculoskeletal pain has increased between 2 and 4 fold in the last forty years (Harkness et al, 2005) and is expected to continue rising with increases in life expectancy and ageing populations (Suka & Yoshida, 2009).

1.4 Widespread musculoskeletal pain

Musculoskeletal pain is best described as a continuum, ranging from at one end those persons reporting no pain, through those reporting pain at single sites, to those at the other end reporting widespread pain. Importantly, chronic pain in a single site is relatively rare. In a population based study in the UK, musculoskeletal pain was assessed in 2,449 participants aged between 18 and 102 years. Of the 618 (25%) participants with chronic lower back pain, 540 (87%) also reported pain in at least one other site (Carnes et al, 2007). The focus of this thesis is the phenotype of widespread musculoskeletal pain (hereafter referred to as widespread pain). Widespread pain can be acute, arising immediately following widespread injury (Holm et al, 2007), however, widespread pain is usually associated with chronicity. Approximately 83% of individuals with widespread pain meet the IASP definition for chronic pain (McBeth et al, 2003).

In order to assess the prevalence of widespread pain it is first necessary to examine the different methods by which it has been conceptualised and three approaches are described in the following subsections. First is the concept of chronic widespread pain (CWP), secondly fibromyalgia (FM) and finally the use of the count of the number of painful sites.

1.4.1 Chronic widespread pain

The American College of Rheumatology (ACR) define CWP as pain present in at least two contralateral body quadrants and the axial skeleton, which has persisted for at least 3 months (Wolfe et al, 1990). As Table 1.1 shows, using the ACR definition gives a community point prevalence of approximately 10% (Papageorgiou et al, 2002) - 19% (Hauser et al, 2012). Similarly, two 15 month prospective community studies found the new onset of CWP to be approximately 9 – 10% using the ACR definition (Nicholl et al, 2009; Gupta et al, 2007). However, studies also obtain similar prevalence rates when not assessing for chronicity (Branco et al, 2010; Macfarlane et al, 2001). For example, Branco et al (2010) used the London Fibromyalgia Epidemiology Study Screening

Questionnaire (LFESSQ-4) to assess the prevalence of widespread pain across Europe. The LFESSQ-4 contains four questions relating to pain which meet the location criteria for the ACR definition, but asks participants to report pain lasting greater than one week in the last three months. They obtained an overall point prevalence of 13%, with figures varying from 10% in Italy and France, to 23% in Spain.

Similarly, meeting the ACR location criteria, but for pain lasting greater than one day in the past month, Macfarlane et al (2001) obtained a point prevalence of 15%. Therefore, the research evidence suggests that the assessment of chronicity does not necessarily influence prevalence estimates at a population level.

Other assessment criteria have also been used to define CWP. The Manchester definition for CWP (CWP-M) is a more stringent criterion of assessment, requiring pain to be present in at least two sections of two contralateral limbs. By stipulating that pain be more widespread, the use of this definition reduces point prevalence to around 4.5 – 4.7% (Bergman, 2005; Hunt et al 1999). Using the CWP-M definition but without an assessment of chronicity, Thomas et al (2004a) reported a point prevalence of 12.5%, which was similar to those studies using the ACR definition. One reason why the prevalence was similar even though a more stringent criteria was used could be the older age of the study population (mean age 66.3 years compared to a median age of 42 years in the study by Hunt et al, 1999).

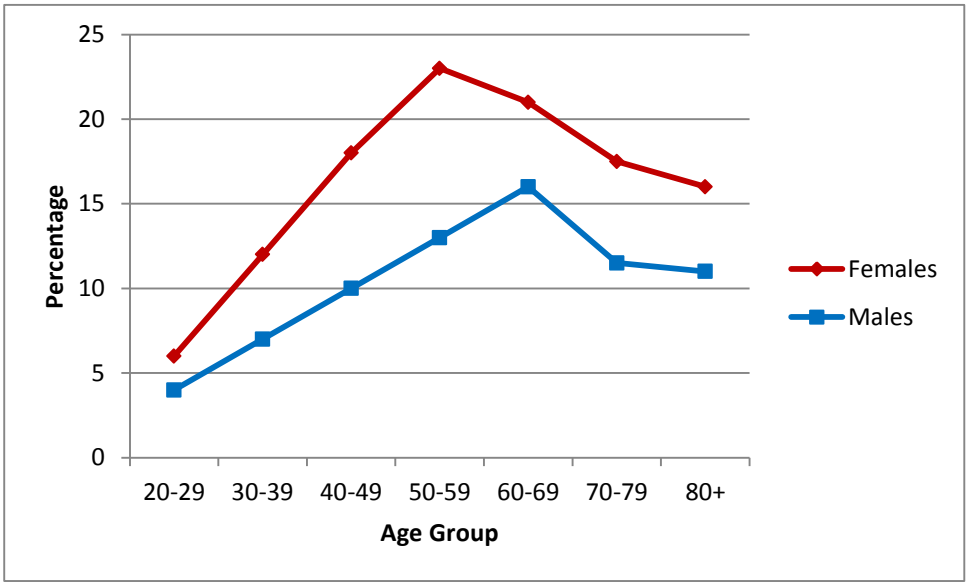
Table 1.1 Community based studies of the point prevalence of widespread pain

Reference	Country	Definition	Sample Size	Point Prevalence (%)
Hunt et al (1999)	UK	ACR	1,953	12.9%
Bergman et al (2002)	Sweden	ACR	2,445	12.0%
Papageorgiou et al (2002)	UK	ACR	1,386	10.0%
Bergman (2005)	Sweden	ACR	2,425	12.5%
Aggarwal et al (2006)	UK	ACR	2,299	15.0%
Carnes et al (2007)	UK	ACR	1,922	11.2%
McBeth et al (2010)	UK	ACR	2,182	17.5%
Santos et al (2010)	Brazil	ACR	361	14.1%
Hauser et al (2012)	Germany	ACR	773	19.0%
Macfarlane et al (2001)	UK	ACR location, duration[1]	6,569	15.0%
Branco et al (2010)	France	ACR location, duration[2]	1,014	10.0%
Branco et al (2010)	Germany		1,002	11.0%
Branco et al (2010)	Italy		1,000	10.0%
Branco et al (2010)	Portugal		500	13.0%
Branco et al (2010)	Spain		1,001	23.0%
Branco et al (2010)	Europe[3]		4,517	13.0%
Bergman (2005)	Sweden	Manchester	2,425	4.5%
Hunt et al (1999)	UK	Manchester	1,953	4.7%
Thomas et al (2004a)	UK	Manchester location, duration[4]	7,878	12.5%
Svebak et al (2006)	Norway	ACR duration, location[5]	64,690	12.6%

[1]Duration - pain lasting > 1 day in past month; [2]Duration - pain lasting > 1 week in past 3 months; [3]France, Germany, Italy, Portugal, Spain; [4]Duration - pain lasting ≥ 1 day in past 4 weeks; [5]Location – axial skeleton, above and below waist

Using less stringent criteria, Svebak et al (2006) assessed the one-year prevalence of CWP in a community sample of 64,690 adults. Although achieving prevalence rates similar to those using the ACR definition (12.6%), they did not meet the pain location criteria of the ACR as their participants were not required to distinguish between pain in the left and right sides. Using their data, Figure 1.1 shows how the one year prevalence of widespread pain increases with age up until approximately 50-59 years for females and 60-69 years for males, with a female predominance at all ages.

Figure 1.1 Prevalence of widespread pain by age and sex



From Svebak et al (2006)

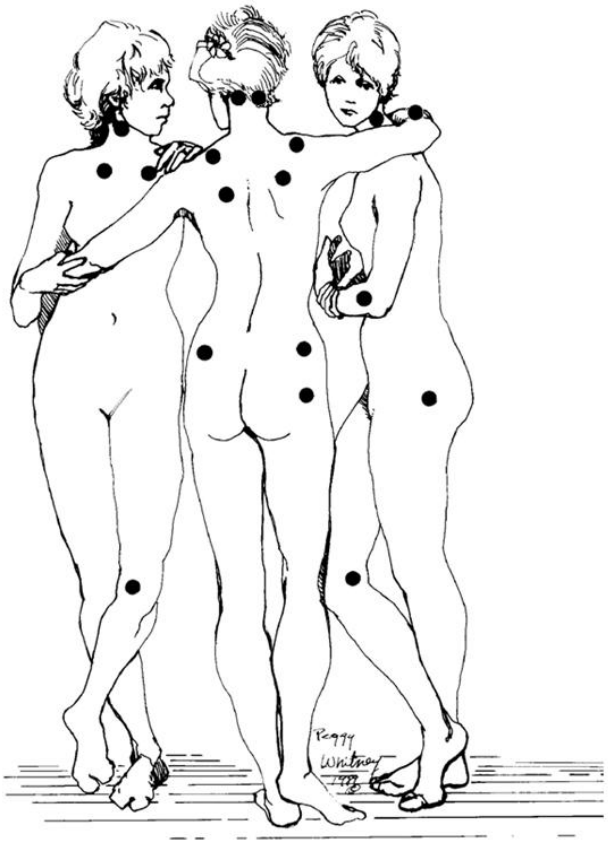
Taking all the evidence together, the population point prevalence rate for CWP as measured using the ACR criteria was approximately 10-19%. The prevalence of widespread pain does not appear to be majorly influenced by the establishment of chronicity (i.e. pain lasting for a period of three months or more). For example, when the ACR location criteria were used, with a pain duration of greater than one day in the previous four weeks (Thomas et al, 2004a) or the previous month (Macfarlane et al, 2001), population point prevalence rates of 12.5% and 15% respectively were obtained. However, prevalence is lower when a more stringent criterion is applied to assess the

location of pain (e.g. CWP-M). Furthermore, evidence shows that the prevalence is generally higher in females and rises with age, reaching a peak at ages 50 to 69 years.

1.4.2 Fibromyalgia

At the extreme end of the chronic musculoskeletal pain continuum is fibromyalgia (FM). FM is widespread pain in the presence of other somatic symptoms, including fatigue, sleep disturbances, headache and irritable bowel (Wolfe et al, 2010). FM also includes the perception of previously innocuous stimuli as painful (allodynia) and reduced pain thresholds (hyperalgesia) (Arnold et al, 2011). The 1990 ACR criteria for FM requires CWP lasting for three months, with pain in at least 11 of 18 tender point sites on palpation (Figure 1.2) (Wolfe et al, 1990).

Figure 1.2 Tender points



Source: Wolfe (2013)

The ACR 1990 criteria for FM provides a population prevalence estimated at between 0.2% and 5.5% (Alvarez-Nemegyei et al, 2011; Santos et al, 2010), as shown in Table

1.2. The LFESSQ-4 was used in the assessment of FM by both Branco et al (2010) and Perrot et al (2011). Branco et al (2010) assessed the accuracy of the LFESSQ-4 by performing physical examinations on 1,125 rheumatology patients. The resulting positive-predictive values were then used to calculate the prevalence of FM in their community sample. Physical examinations were also performed on a subset of 96 participants by Perrot et al (2011). This method gave a prevalence ranging from 1.6% (Perrot et al, 2011) to 6.6% (Branco et al, 2010). Studies using a self-report of a physician diagnosis of FM obtain prevalence rates of 1 – 2% (for example, Fuller-Thompson et al, 2012; Kurtze & Svebak, 2005). Both Branco et al (2010) and Santos et al (2010) assessed CWP and FM in the same participants, showing that approximately 10% of individuals with CWP meet the FM ACR 1990 criteria.

The 1990 ACR Criteria did not take into account the importance of non-pain related symptoms that have been subsequently associated with FM (Wolfe et al, 2010). Also the reliability (Bidari et al, 2009), validity (Wolfe, 2003) and use of tender point counts have been hotly debated (Fitzcharles & Yunus, 2012; Harth & Nielson, 2007). An alternative diagnostic method has therefore recently been proposed to better reflect the growing understanding of FM (Wolfe et al 2010; 2011). This new criteria (ACR 2010) comprise a Widespread Pain Index and a Symptom Severity Scale, and removes the tender point examination (Wolfe et al, 2010). The Widespread Pain Index assesses the number of painful sites (out of 19), whilst the Symptom Severity Scale evaluates the extent and severity of fatigue, sleep, cognitive problems and somatic symptoms. The ACR 2010-M is a modified version of the ACR 2010 criteria which allows for self-administration (Wolfe et al, 2011). Using these criteria, Vincent et al (2013) obtained a community prevalence of 6.4%.

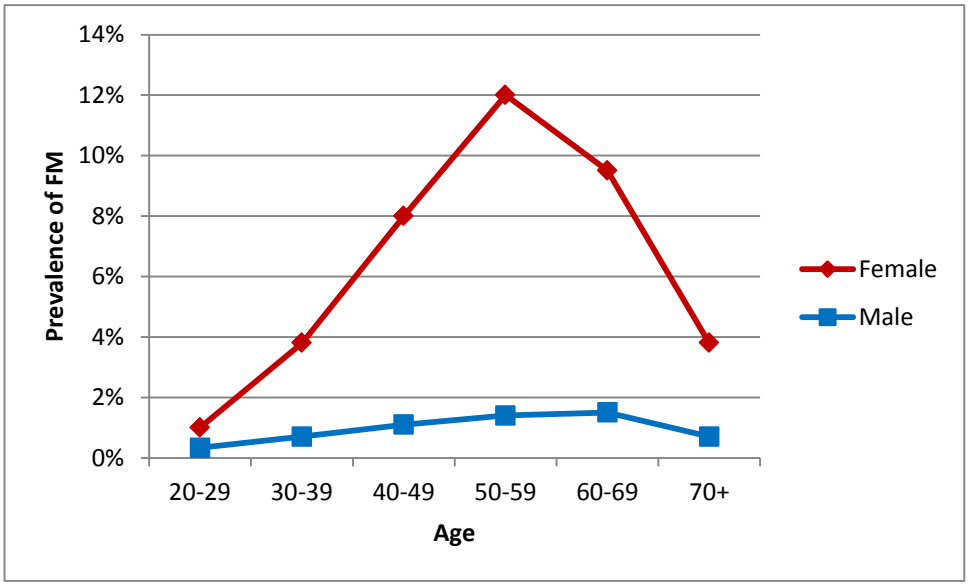
Table 1.2 Community based studies of the point prevalence of Fibromyalgia

Reference	Country	Definition	Sample Size	Point Prevalence (%)
Santos et al (2010)	Brazil	ACR 1990	361	5.5%
Alverez-Nemegyei et al (2011)	Mexico	ACR 1990	3,915	0.2%
Branco et al (2010)	France	LFESSQ-4[1]	1,014	2.2%
Branco et al (2010)	Germany		1,002	5.8%
Branco et al (2010)	Italy		1,000	6.6%
Branco et al (2010)	Portugal		500	3.7%
Branco et al (2010)	Spain		1,001	4.0%
Branco et al (2010)	Europe[2]		4,517	2.9%
Perrot et al (2011)	France	LFESSQ-4[3]	3,081	1.6%
Wenzel et al (2009)	Norway	Self-report of diagnosis	55,046	2.0%
Fuller-Thompson et al (2012)	Canada	Self-report of diagnosis	126,805	1.1%
Vincent et al (2013)	USA	ACR 2010-M	830	6.4%

[1]London Fibromyalgia Epidemiology Study Screening Questionnaire using positive predictive values from tertiary care patients; [2]France, Germany, Italy, Portugal, Spain; [3]London Fibromyalgia Epidemiology Study Screening Questionnaire and confirmation of diagnosis by examination

As with CWP, a female predominance exists with FM. Point prevalence rates for males range from 0.9% (Kurtze & Svebak, 2005) to 3.8% (Branco et al, 2010 – Italy) whilst in females the prevalence ranges from 2.6% (Branco et al, 2010 – France) to 9.8% (Branco et al 2010 – Italy). Figure 1.3 shows the prevalence of FM by age and sex in a community based Norwegian study. Overall, a physician diagnosis of FM was self-reported by 0.9% of males and 5.2% of females, with a peak at approximately 50-59 years for females (12%) and 60-69 years for males (1.4%) (Kurtze & Svebak 2005).

Figure 1.3 Self-reported prevalence of clinician diagnosed fibromyalgia by age and sex



Source: Kurtze & Svebak, 2005

The population point prevalence rate for FM ranges from 0.2% to 6.6%. Approximately 10% of individuals with CWP also meet the ACR 1990 criteria for FM. As would be expected, the evidence shows that FM has a female predominance and prevalence increases up until approximately age 69 years.

1.4.3 Number of pain sites

The ACR criteria, described above, are used for classification, therefore giving a dichotomous outcome – either an individual meets the criteria at a particular point in

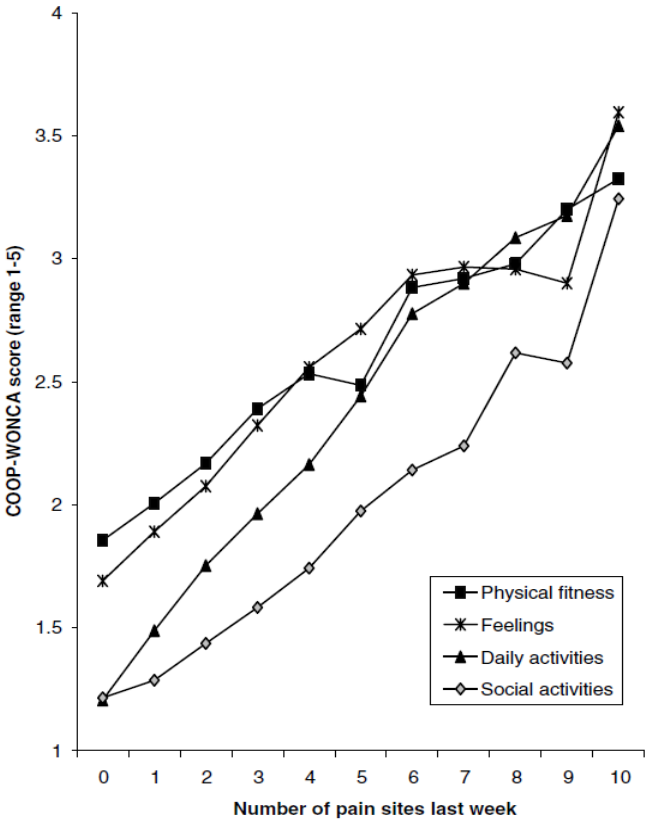
time, or they do not. Research suggests that symptoms develop gradually and fluctuate throughout the day, from day to day, and seasonally (Prince et al, 2000). Not all individuals with widespread pain meet the ACR criteria (Carnes et al, 2007). Even if they do not meet the criteria, they are still in pain. Whilst the concepts of CWP / FM are useful for aligning treatment based on diagnosis, the cut off points are, in effect, arbitrary (Natvig et al, 2010). A third method of assessing widespread pain is by counting the number of sites in which an individual experiences pain. It could be argued that this method offers a more practical way to assess the pain experience, being more reflective of that experience in the population (Natvig et al, 2010). Furthermore having a more sensitive measure of widespread pain allows for the assessment of the potential relationships between risk factors, which is the central topic of this thesis.

Whilst the number of pain sites is a potentially more useful way to examine the relationship between risk factors compared to the dichotomous criteria of CWP or FM, the ACR criteria does provide a standardised measure for assessing widespread pain. With regard to the number of pain sites, studies do vary in the number of sites of pain assessed. As a consequence prevalence rates vary making comparisons between studies difficult. For example, both Sullivan et al (2009) and Holm et al (2007) asked participants to shade the location of their pain onto blank pain manikins. Sullivan et al (2009) examined four sites of pain; back, neck, upper and lower extremity pain, whilst Holm et al (2007) divided the body into 45 individual sites. Measures that assess a higher number of pain sites provide a finer granularity of data, allowing for more detailed and thus more informative analysis (MacCallum et al, 2002).

Kamaleri et al (2008a) examined pain in ten sites. They collected information from 3,179 participants aged 24 to 76 years old regarding the number of sites in which they had experienced pain in the last seven days. Pain in five or more sites was reported by 17.3% of participants, with 2.5% reporting pain in nine or more sites. A strong linear relationship between number of pain sites and poor outcomes was found using a COOP-

WONCA chart. COOP-WONCA charts, developed by the Dartmouth Primary Care Cooperative Research Network (COOP) and the World Organization of National Colleges, Academies, and Academic Associations of General Practitioners / Family Physicians (WONCA), measure aspects of functional ability, with higher scores indicating greater limitations (van Weel et al, 2012). The graph in Figure 1.4 shows the relationship between number of pain sites and four aspects of functional ability - physical fitness, mood, daily and social activities. This research clearly illustrates that as the number of pain sites increase there is also a corresponding increase in the limitations for the individual.

Figure 1.4 Number of pain sites and limitations in functioning



Source: Kamaleri et al, 2008a

When compared to individuals with regional pain, those with widespread pain report greater interference of pain on their general activity, relationships with others and their enjoyment of life (Burckhardt & Jones, 2005). The number of pain sites has also been shown to predict work absenteeism over a seven year period (Haukka et al, 2013).

In summary, there are different ways in which widespread pain has been assessed (CWP using the ACR and Manchester criteria, FM using ACR criteria and a simple count of the number of sites of pain). Despite this variation, the prevalence range is broadly similar at approximately 10% to 23%. It is also clear from the Kamaleri et al (2008a) study and other studies (Bergman, 2005; Burckhardt & Jones, 2005; Haukka et al, 2013) that the physical and psychological impact of pain on the individual increases as the pain becomes more widespread.

1.5 Public health burden of widespread pain

As demonstrated above, widespread pain is common in the community, in many geographical locations (i.e. Europe and North and South America) and has a detrimental impact on the individual (Kamaleri et al, 2008a; Burckhardt & Jones, 2005; Haukka et al, 2013). However, the impact is not just on the individual; widespread pain also has implications for family and friends, who may be relied upon for practical, psychological and financial support (Arnold et al, 2008); for employers due to reduced productivity, sick leave and early disability retirements (Stewart et al, 2003); and for society, in the form of increased health care utilisation and disability costs (Berger et al, 2007). For example, gross expenditure for 2010 / 2011 by the National Health Service (NHS) in England is estimated at £5.06 billion for musculoskeletal conditions. This compares with £2.24 billion for coronary heart disease, £5.81 billion for cancer, and £11.91 billion for mental health disorders (Department of Health, 2011). Musculoskeletal conditions account for approximately 20% of incapacity benefit claims, adding further economic costs in the region of £20 billion (Phillips, 2009).

1.6 Conclusion

This chapter has demonstrated that there are clear differences between acute and chronic pain and that pain has a dual nature. Pain is a symptom of underlying pathology that needs to be addressed, but also pain has symptoms of its own. Chronic pain is thus

a condition in its own right that can be considered as a public health problem. The central focus of this thesis was to examine the aetiology of widespread musculoskeletal pain; the most common form of chronic pain. Three methods of conceptualising widespread pain have been described and research evidence has been presented suggesting that 10% to 23% of individuals are affected by widespread pain. The similarity of these prevalence rates between studies regardless of whether or not they include an assessment of the duration of pain, suggests that the majority of widespread pain is associated with chronicity (for example, Bergman, 2005; Thomas et al, 2004a; Aggarwal et al, 2006 and Macfarlane et al, 2001).

Chapter 2 Background: Trauma, stress and pain

2.1 Chapter overview

Chapter one described the epidemiology of widespread pain and demonstrated the considerable burden to both individuals and society resulting from widespread pain. In order to design and implement effective risk reduction and treatment strategies it is essential that the aetiology and mechanisms of the development and persistence of widespread pain are identified and understood. Widespread pain is a disorder with a complex aetiology. Individuals with widespread pain report the experience of childhood abuse and physical trauma in adulthood more frequently than healthy individuals (Ruiz-Perez et al, 2009; Bennett et al, 2007). However, evidence of a direct link between trauma and widespread pain is inconsistent; some research reports significant associations, whereas others do not. Psychological stress, on the other hand, has been consistently implicated in the development and persistence of widespread pain (Gupta et al, 2007; Gale et al, 2012; McBeth et al, 2001a; c). However, not everyone who experiences psychological stress goes on to develop widespread pain (Gupta et al, 2007; Amital et al, 2006). This suggests that some individuals may be more susceptible to developing widespread pain than others, when they become stressed. This thesis hypothesises that traumatic experiences may create such susceptibility. It is proposed that the inconsistency within the literature with regard to trauma and widespread pain may be explained by the way the relationship has been conceptualised and examined. For example, the majority of previous research has explored a direct association (i.e. trauma to pain), without considering the role of psychological stress, which has already been identified as a significant factor. In order to address this issue, a theoretical model has been developed that examines the relationship between trauma, stress and pain in a different way; using a diathesis stress framework. It is argued that by exploring the moderators (in whom) and mediators (mechanisms) of the stress pain relationship, this model has the potential to identify susceptible individuals and also the psychological and social processes that could be targeted in treatment.

Section 2.2 of this chapter considers the role of trauma in the development and persistence of widespread pain. Following a definition of trauma, previous research examining a direct association between trauma and widespread pain is systematically reviewed. The role of psychological stress in the development and persistence of widespread pain is examined in Section 2.3. A definition of psychological stress is presented, followed by an overview of the research evidence. An outline of existing theoretical models of trauma and widespread pain is presented in Section 2.4. Section 2.5 then introduces the trauma diathesis model of widespread pain. Each component of the trauma diathesis stress model of widespread pain is described and examined in turn. Following a summary of currently available treatments for widespread pain, this chapter concludes with the rationale for this thesis.

2.2 Trauma and widespread pain

The role of trauma in the development and persistence of widespread pain is the central enquiry of this thesis. Following a definition and history of trauma, this section provides a review of the literature associating trauma with widespread pain.

2.2.1 Trauma: Definition and history

A traumatic event is defined as *"actual or threatened death, serious injury, or sexual violation" (DSM-V, 2013) that "is extremely upsetting and at least temporarily overwhelms the individual's internal resources."* (Briere & Scott, 2006, pg4). The long term psychological implications of the exposure to traumatic events, including childhood abuse, combat, disasters and accidents, have long been recognised (Banyard et al, 2009a). Such events challenge an individual's previously accepted world views, and their sense of self and identity (Agaibi & Wilson, 2005; Berntsen & Rubin, 2007). The experience of trauma is often associated with a perception of a loss of control, which along with the unpredictability of the event, highlights an individual's vulnerability (Salcıoglu & Basoglu, 2008).

The consequences of trauma on physical health are the subject of a long running debate (Raphael et al, 2004). Hysteria and somatic complaints were recognised as long term consequences of childhood maltreatment by the French psychiatrists Briquet in 1859 (van Der Kolk et al, 2007b) and Tardieu in 1860 (Labbe, 2005), and by Freud in 1896 (Freud, 1897). Around this time, in 1874, the New York Society for the Prevention of Cruelty to Children was established. This was the first organisation concerned with the protection of children, and was closely followed in 1889 by the development of the National Society for the Prevention of Cruelty to Children (NSPCC) in England (Myers, 2008). However, the retraction of his Seduction Theory (Freud, 1897), when Freud dismissed the majority of reports of abuse as fantasy (Freud, 2010), resulted in the disbelief of histories of abuse and interest in the topic waned (Labbe, 2005). The early studies by Briquet and Tardieu illustrated the wide prevalence and detrimental impact of childhood abuse; however, the issue was not included on the agenda of mental health and child welfare professionals until the mid-1970s (Finkelhor, 1986).

Significant advances in trauma research were made in the study of combat, when symptoms similar to hysteria were described by military combat personnel. Such conditions include Soldier's Heart and DeCosta's syndrome from the American Civil war (Friedman et al, 2011; Wood, 1941), Shell Shock from the First World War (Jones & Wessely, 2007), Kardiner's traumatic neuroses of war from World War Two (Dayan & Olliac, 2010) and more recently Gulf War syndrome (Iversen et al, 2007). Combat related research was instrumental in the development of PTSD, the diagnosis of which was included in the DSM, third edition by the American Psychiatric Association in 1980 (Brett, 2007).

With regard to accidents and injuries, the first disaster psychiatrist, Stierlin, studied the impact of civilian trauma, including a mining disaster in 1906 and an Italian earthquake in 1907. Finding that 25% of the earthquake survivors suffered from sleep disturbances and nightmares, Stierlin recognised that such reactions were not rare or atypical (van der

Kolk et al, 2007b). In addition to these traumatic events which affect whole communities, accidents and injuries affecting individuals have also been found to elicit traumatic reactions (Tolin & Foa, 2006). Events typically studied in this regard include road traffic accidents (RTA) (Mayou & Bryant, 2001; Gudmundsdottir & Beck, 2004), surgery (Osterman et al, 2001), hospitalisations (Haagsma et al, 2012), time spent in intensive care (O'Donnell et al, 2010), fractures and burns (Andreasen & Norris, 1972; Gilboa, 2001).

Research and treatment efforts have mostly focused on psychological and social consequences of trauma (Banyard et al, 2009a). Initially, research findings that many individuals reported traumatic experiences prior to the onset of physical health problems were attributed to hysteria, or disorders of will (van der Kolk, 2007b):

> *"symptoms were viewed as idiosyncratic, written off as primarily psychological in origin, and were generally not of interest to health care providers."* (Kendall-Tackett & Klest, 2009, pg129)

This was because the health conditions concerned were deemed as functional (i.e. physical abnormalities could not be identified) (Kendall-Tackett & Klest, 2009). However, the findings of a relationship between traumatic experiences and a number of recognised physical health problems, such as ischaemic heart disease, cancer, skeletal fractures, stroke and liver disease (Felitti et al, 1998), has widened the scope of research in this area (Kendall-Tackett & Klest, 2009).

This thesis examines two types of traumatic experiences to assess whether they increase an individual's susceptibility to widespread pain: childhood interpersonal trauma, in the form of childhood physical, emotional and sexual abuse and neglect, and adult physical trauma, such as the experience of surgeries, fractures, RTAs and burns. For each of these trauma types, a definition is followed by a review of the literature examining a direct relationship with widespread pain.

2.2.2 Childhood interpersonal trauma

Interpersonal traumatic experiences in childhood include physical, sexual and emotional abuse and neglect. Physical abuse includes

> *"hitting, shaking, throwing, poisoning, burning or scalding, drowning, suffocating, or otherwise causing physical harm to a child"*
>
> (Her Majesty's [HM] Government, 2010, pg38)

Childhood physical abuse can result in physical injury ranging in severity from minor marks to death. Such injury can be the result of a one-off attack or repeated episodes of violent action. Childhood emotional (or psychological) abuse involves the persistent humiliation, terrorising and insulting of a child, such that they are made to feel worthless, unloved, endangered and / or guilty (Radford et al, 2011).

> *"Child sexual abuse is the involvement of a child in sexual activity that he or she does not fully comprehend, is unable to give informed consent to, or for which the child is not developmentally prepared and cannot give consent, or that violates the laws or social taboos of society"*
>
> (World Health Organisation, 2003, pg75)

Such activities include non-contact (for example indecent exposure), contact (for example touching) and penetration (for example rape or oral sex). These acts are classed as sexual abuse regardless of whether or not the child comprehends the situation, and regardless of the level of violence (HM Government, 2010). Childhood neglect involves the failure of a parent or caregiver to provide adequate food, clothing, shelter, supervision and protection from harm. Being unavailable or inattentive to a child's emotional needs and the failure to provide appropriate psychological and medical healthcare are also classed as neglectful (Radford et al, 2011).

a) Prevalence of childhood interpersonal trauma

Childhood abuse and neglect are not rare. The prevalence rates for childhood abuse and neglect vary considerably between studies, ranging from 3% (Department for Education [DfE], 2010) to 65% (Goldberg et al, 1999). This variation is due, in part, to differences in how childhood abuse is measured and the populations being examined. For example, child protection figures show that approximately 2.91 million (4%) children are affected by child abuse and neglect in the USA (Sedlak et al, 2010). Similarly, in 2010, 375,900 children (3.4%) in the UK were classed as "in need" i.e. requiring social services intervention (DfE, 2010). However, these figures, based on official child protection statistics, are likely to be an under-estimate as approximately 50% to 80% of abuse and neglect cases are never reported (Fallon et al, 2010). This is reflected in the findings of a recent NSPCC study in which 19% of the 11 – 17 year olds (n=2,275) and 25% of 18 – 24 year olds (n=1,761) interviewed reported experiencing severe abuse or neglect (Radford et al, 2011). A rate of 43% was obtained in a population based study of 8,667 participants (age range 19 – 97 years, mean age 55 years) (Edwards et al, 2003). The types of childhood abuse and neglect have also been considered individually. For example, in four recent meta-analyses, Stoltenborgh et al (2011; 2012; 2013a; 2013b) examined the prevalence rates for self-reported childhood abuse and neglect in studies published between 1980 and 2008. The overall estimated prevalence was 22.6% for physical abuse, 36.3% for emotional abuse, 12.7% for sexual abuse, 16.3% for physical neglect and 18.4% for emotional neglect. Clearly, studies using self-report measures of childhood abuse and neglect report considerably higher prevalence figures in comparison to official Government literature. The studies, by Radford et al (2011), Stoltenborgh et al (2011; 2012; 2013a; 2013b) and Edwards et al (2003) were all based on non-clinical populations. Studies examining the prevalence of childhood abuse and neglect in clinical populations do report much higher rates. For example, prevalence rates of 54.6% (Haviland et al, 2010), 58.5% (Smith et al, 2010), 51.4% (Carpenter et al, 1998) and 57.9% (Imbierowicz & Egle, 2003) have been obtained for

physical, emotional and sexual abuse and neglect respectively in individuals with widespread pain.

Physical, emotional and sexual abuse and neglect can occur in isolation. However, the co-occurrence of abuse types is very common (Bernstein et al, 2003) with up to 35% of those reporting abuse identifying more than one type (Edwards et al, 2003). For example, Dong et al (2003) compared individuals with and without childhood sexual abuse. Childhood sexual abuse significantly increased the odds of reporting other forms of abuse and neglect: childhood physical (OR 2.0 95% CI 1.7, 2.2), emotional (OR 2.5 95% CI 2.1, 3.0) and neglect (OR 2.0 95% CI 1.6, 2.5).

In summary, prevalence estimates for childhood abuse and neglect vary, with studies using self-report measures obtaining considerably higher figures in comparison with official government statistics. Childhood abuse is a "global problem that has significant consequences for public health" (Radford et al, 2011, pg15). The following two sub-sections examine the research evidence of the long term effects of childhood abuse. Section 2.2.2b below briefly reviews the evidence linking childhood abuse and neglect to physical ill health, in general. Section 2.2.2c considers in more detail the evidence seeking a direct association between childhood abuse and neglect and widespread pain.

b) Childhood interpersonal trauma and ill health

The long term physical health consequences of childhood abuse and neglect have been the subject of four recent literature reviews. Direct associations were identified with general health problems, gastrointestinal, gynecological and reproductive ill health (Irish et al, 2010; Paras et al, 2009; Wegman & Stetler, 2009; Raphael et al, 2004). For example, a meta-analytic review by Wegman & Stetler (2009) found that childhood abuse and neglect increased the risk of 10 different adult medical outcomes. Although childhood abuse and neglect increased the risk of all outcomes considered (number of

symptoms, hospitalisations, cardiovascular disease, diabetes, obesity, respiratory, gastrointestinal, gynecological, neurological and musculoskeletal problems), the strongest relationships where found with neurological and musculoskeletal problems (Wegman & Stetler, 2009).

The detrimental effects of abuse show a dose response, whereby multiple types of abuse and frequently occurring abuse lead to greater levels of traumatisation (Clemmons et al, 2007). Such a dose response has been shown to result in increasingly poorer mental and physical health (Edwards et al, 2003). For example, in a community study including 1,912 females, the number of types of abuse reported was significantly associated with the number of self-reported physical symptoms and the number of physician diagnoses for infectious diseases, mental health problems and pain disorders, obtained from medical records (Walker et al, 1999).

With regard to pain, three prospective studies assessing associations with childhood abuse and neglect have been identified. Brown, Berenson & Cohen (2005), assessing both court documented and self-reported abuse and neglect, found that chronic pain was associated with self-reported childhood sexual abuse, but not with self-reported or documented physical abuse or neglect. Raphael et al (2001; 2011) compared pain symptoms and pain problems between individuals with court documented childhood abuse occurring before age 11 and a comparison cohort matched for age, race, gender, and approximate parental socioeconomic status. No association was found between documented abuse and the number of pain symptoms or problems with pain at the initial follow up (mean age 29.1 years, standard deviation 3.8) (Raphael et al, 2001). However, at subsequent follow up (mean age 41.2 years, standard deviation 3.5) additional analysis was performed to investigate the potential effects of PTSD measured at initial follow up. PTSD did not mediate the relationship between childhood abuse and pain, however, a moderation effect was found. Participants with both a

history of abuse and PTSD had a significantly increased risk of pain symptoms and pain problems than those with documented abuse or PTSD alone (Raphael et al, 2011).

Five literature reviews have been identified which assessed direct associations between childhood abuse and chronic pain (Hauser et al, 2011; Paras et al 2009; Romans & Cohen, 2008; Davis et al, 2005; Raphael et al, 2004). The evidence from each review is suggestive of a link between childhood abuse and physical health problems; however, each conclude that the wide variation between studies and methodological issues in study design prevent firm conclusions from being drawn.

c) Childhood interpersonal trauma and chronic widespread pain

Although four of the recent literature reviews referred to above included FM as an outcome (Hauser et al, 2011; Paras et al, 2009; Romans & Cohen, 2007; Raphael et al, 2004), to date no review has been identified which examines the association between childhood abuse and the broader concept of widespread pain. Therefore, a systematic search of the databases MEDLINE, EMBASE, psychINFO, CINHAL, AMED, BNI and web of knowledge was performed. The search terms included all MESH and thesaurus terms relating to “adult” AND "fibromyalgia" or “fibrositis” or "FM" or "FMS" or "chronic pain" or "chronic widespread pain" or "CWP" AND “child” or “childhood” AND "abuse" or "trauma" or "interpersonal abuse" or "early life" or "sexual abuse" or "psychological abuse" or "emotional abuse" or "physical abuse" or "incest" or "neglect" or "life events" or "victimisation" or "victimization" or "maltreatment” or “rape” or “bullying” or "adversity". The references of included articles and relevant systematic reviews were also manually checked to identify further papers. Studies were included if they examined trauma types individually or in any combination.

Table 2.1 Associations between widespread pain and FM and childhood abuse and neglect

Year	Author	Method	Outcome	Childhood abuse	Childhood abuse type			
					Physical	Emotional	Sexual	Neglect
2001c	McBeth et al	Cross-sectional	CWP	-				
2001	Van Houdenhove et al	Case control	CFS/FM	-				
2005	Castro et al	Case control	FM	+ / -				
2009	Ruiz-Perez et al	Case control	FM	+	-	-	-	
2000	Anderberg et al	Case control	FM		-		-	-
2005	Ciccone et al	Case control	FM		-		-	
1999	Goldberg et al	Case control	FM		-	-	-	
1995	Boisset-Pioro et al	Case control	FM		+		+	
1998	Carpenter et al	Case control	FM		+		+	
2011	Fuller-Thomson et al	Cross-sectional	FM		+			
2010	Haviland et al	Cross-sectional	FM		+			
2003	Imbierowicz et al	Case control	FM		+		+	+
2010	Smith et al	Case control	FM		+	+	+	
1997	Walker et al	Case control	FM		-	-	-	+
2000	Finestone et al	Cross-sectional	FM				+	

FM = fibromyalgia; CWP = chronic widespread pain; + = significant associations; - = non-significant associations; + / - =mixed findings

Fifteen studies were identified which reported an outcome of widespread pain in adults (18 years of age or over) with a predictor of physical, emotional or sexual abuse or neglect occurring in childhood (18 years or less), as shown in Table 2.1. Whilst validated and reliable measures of CWP / FM were used in all 15 studies, variations were found in the assessment of childhood abuse, in the use of multivariable analysis and in the populations examined. Further details of the study characteristics are presented in Table A1.1 in Appendix 1.

(i) Assessment of childhood abuse

There was considerable variation in the types of childhood interpersonal trauma investigated. Four studies considered the overall effect of childhood abuse, two of which report no association with widespread pain (McBeth et al, 2001c; Van Houdenhove et al, 2001), whilst two report an association (Castro et al, 2005; Ruiz-Perez et al, 2009). The two studies finding an association both assessed physical, sexual and emotional abuse, whilst those not finding an effect also included neglect. This could suggest that the inclusion of neglect weakens any effect of the other abuse types. However, two of the three studies specifically examining neglect as a distinct abuse type did find significant associations with widespread pain (Imbierowicz et al, 2003; Walker et al, 1997). Only two of the studies examined all four types of childhood abuse (Walker et al, 1997; Anderberg et al, 2000).

The measures used to assess childhood abuse varied with regard to the age prior to which childhood abuse occurred. One study assessed childhood abuse before age 11, two prior to age 14 years, four prior to age 16 and two prior to age 18. Six studies did not specify what age was used. Significant associations were found in those studies assessing childhood abuse in younger age groups. For example, Castro et al (2005) found a significant association between FM and abuse occurring prior to age eleven, but not between ages twelve to fifteen years, whilst Carpenter et al (1998) found a significant association between FM and both physical and sexual abuse

occurring prior to age 14 year. Both studies using the upper age limit of 18 years found no association between physical, emotional or sexual abuse and FM (Goldberg et al, 1999; Walker et al, 1997). This would suggest that childhood abuse occurring earlier in childhood may have a greater detrimental effect on health than abuse occurring later in childhood.

Only one study included an assessment of the frequency of childhood abuse. Ruiz-Perez et al (2009) compared the prevalence of childhood abuse between 287 female patients with FM (cases) and 287 female ear nose and throat (ENT) patients without FM (controls). Participants were asked if they had been physically, emotionally or sexually abused during childhood never, once, sometimes or many times. For each abuse type, a participant was classed as abused if she gave a positive response (once, sometimes or many times). When considering the three types of abuse individually and dichotomised in this way, there was no significant difference in prevalence between the two groups. However, FM patients were twice as likely to report experiencing frequent (sometimes or many times) abuse of any type than the ENT patients. This provides further evidence for a dose response to childhood abuse and neglect. The results of this research also suggest that the use of a more sophisticated measure of abuse, including an assessment of severity (or frequency), would provide greater insight into the role of childhood abuse in the development of widespread pain than a dichotomised measure.

(ii) Issues of analysis

Nine of the studies included in Table 2.1 considered only the prevalence of self-reported childhood abuse in their analysis. Of these, seven studies found that childhood abuse was reported more frequently by individuals with widespread pain than by patients with rheumatoid arthritis (Castro et al, 2005; Carpenter et al, 1998), non-FM rheumatic disease (Boisset-Pioro et al, 1995), medically explained pain (Imbierowicz et al, 2003), psychiatric disorders (Finestone et al, 2000), ear nose and

throat complaints (Ruiz-Perez et al, 2009) and healthy controls (Castro et al, 2005; Smith et al, 2010; Finestone et al, 2000). In these studies no consideration was given to any other factors known to be associated with widespread pain. In contrast, six studies used multivariable analysis to take account of such factors. Three of these studies found no association between widespread pain and childhood abuse. McBeth et al (2001c) interviewed 296 participants in a community based study. Although childhood abuse was reported more frequently by participants meeting the ACR criteria for CWP compared to those without pain (11.9% and 2.3%, respectively), this difference was not significant in multivariable analysis controlling for age and sex (OR 4.8 95% C.I. 0.8 to 27.4). Similarly, Ciccone et al (2005) found no significant difference in self-reported childhood physical or sexual abuse between females with and without FM, when controlling for age and education. However, the females without FM "were not necessarily pain free" (Ciccone et al, 2005, pg379); they simply did not meet the ACR criteria for FM at the time of assessment. Goldberg et al (1999) compared physical, verbal and sexual abuse in patients diagnosed with FM, facial, myofascial and other chronic pain (including low back pain, neck pain and spinal pain). Abuse did not predict membership of the four pain groups when controlling for pain intensity, pain disability, medication use and sleep disorders. However, this study did not include a pain free group for comparison; comparisons were made between the "other" pain group and the specific conditions of FM, facial and myofascial pain. These results could therefore be taken to suggest that childhood abuse is not specifically associated with FM, but that a relationship exists with chronic pain in general.

Two studies which did find an effect using multivariable analysis were community based studies examining the association between FM and childhood physical abuse. Haviland et al (2010) accounted for age, race, income and education. The study by Fuller-Thomson et al (2011) was the only one to take account of stress as well as demographic factors, when including a healthy participant comparison group. They

controlled for age, race, childhood stressors, adult health behaviours, adult socio-economic status and stressors, and mental health when assessing the relationship between physical abuse and FM in 7,342 females. Walker et al (1997) compared the frequency of self-reported childhood abuse and neglect in 32 female FM patients and 28 female rheumatoid arthritis patients. In their univariate analysis, FM was associated with physical, emotional and sexual abuse and emotional neglect. However, although the abuse and neglect scores from their questionnaire correctly classified 70% of the patient's diagnoses (rheumatoid arthritis vs FM) when entered into a logistic regression, only neglect made a significant contribution to the prediction.

(iii) Study populations

In nine of the 15 studies the study population was 100% female participants. Of the six studies including male participants, three (50%) found a significant association between childhood abuse and widespread pain (Castro et al, 2005; Haviland et al, 2010; Imbierowicz et al, 2003) and three did not (McBeth et al, 2001c; Van Houdenhove et al, 2001; Goldberg et al, 1999). In contrast, seven (78%) of the nine all female studies found significant associations. This suggests that the relationship between childhood abuse and widespread pain may be different in males and females. This is discussed more fully below (Section 2.5.3ii, pg68).

(iv) Quality and risk of bias assessment

An assessment of the quality and risk of bias within these studies was carried out using a quality and risk assessment tool developed jointly by the author and Dr Paul Campell. Appendix 1 describes how the tool was developed and used to assess the quality / risk of bias within these fifteen studies.

The results of the quality / risk assessment of contained in tables A1.2 to A1.6 in Appendix 1. Overall, studies reporting no association between childhood abuse and CWP outcomes employed stronger methodological rigour compared to studies who did

report associations, suggesting that findings of no effect are more robust. Only those studies reporting an association between childhood neglect and CWP employed stronger methodological rigour compared to the study that did not report an association. However, the small number of studies considered and the overall low quality / high risk of bias (compared to other abuse types) in these studies prevent firm conclusions from being reached.

The main difference between the studies finding an association and those that did not was with regard to participation. Overall the differences were mainly related to the failure of studies finding an effect to clearly describe their inclusion / exclusion criteria, report response rates and provide a clear analysis of the difference between responders and non-responders. This, however, may reflect quality of reporting rather than quality of methodology.

Overall, ten of the fifteen studies (Table 2.1) found significant associations between widespread pain and childhood abuse and neglect. Significant associations were found between widespread pain and physical abuse in six (55%) studies, emotional abuse in one (25%) study, sexual abuse in five (50%) studies and neglect in two (67%) studies and childhood abuse in general in two (50%) studies. However, study quality was generally lower in those studies finding a significant association. It is proposed that this inconsistency is due not only to the differences in study quality, but also to the lack of consideration of the role of psychological stress, the way in which the relationship was examined and the populations studied. The trauma diathesis stress model of widespread pain, presented in Section 2.5, proposes a direct relationship between psychological stress and widespread pain, moderated by childhood abuse and sex. Only two of the fifteen studies (Fuller-Thomson et al, 2011; Goldberg et al, 1999) included psychological stress in their analysis, all fifteen studies explored a direct link between childhood abuse and widespread pain and none of the studies examined whether the relationships were different in males and females.

This section has examined the research exploring a direct association between childhood abuse and widespread pain. The following section examines the relationships between adult physical trauma and widespread pain.

2.2.3 Adult physical trauma

Along with childhood interpersonal trauma, individuals with widespread pain frequently report precursory physically traumatic experiences. In an internet survey completed by 2,569 individuals with FM, 78% identified a triggering event for their illness. Events included acute illness (27%), RTA (16%), physical injury not related to RTA (17%) and surgery (16%) (Bennett et al, 2007). This thesis focuses on the traumatic experiences of surgery, fractures, RTA and burns occurring during adulthood. These events were chosen based on the current literature.

a) Prevalence of adult physical trauma

Physically traumatic experiences are common. Over 4.6 million hospital admissions result in surgery each year in the UK (Royal College of Surgeons, 2012), including 60,000 hysterectomies and around 7% of the population require an appendectomy at some point (NHS, 2013). Although in general, medical conditions tend to become more common with age, the rate of surgical treatment declines over the age of 65 years of age (Royal College of Surgeons, 2012). The incident rate for fractures was approximately 3.6 per 100 people per year in 2004 (England only) (Donaldson et al, 2008). For males, the highest incident rate is for children aged 0 – 4 years (7.7 per 100). This rate then declines with age. For females, however, the highest incident rate occurs in the over 55 year olds (7.6 per 100).

> *"The peak incidence of fracture in males and females was thus similar in magnitude but occurred at different ends of the age spectrum"*
>
> (Donaldson et al, 2008, pg174)

There were approximately 730,000 road traffic casualties in the UK in 2012 (Department of Transport, 2013a), which equated to approximately 1.2% of the UK population (Office for National Statistics [ONS], 2012). The majority of these accidents (75%) involved individuals aged between 17 to 59 years of age, with 12% involving individuals over 60 years of age (Department of Transport, 2013b). Approximately 26 per 10,000 people experience burns each year (McCormick et al, 1995). The highest incidence of burns occurs in under four year olds (68 per 10,000), after which incidence reduces to around 20 per 10,000, until age 85, when the rate increases again to 43 per 10,000 (McCormick et al, 1995).

b) Adult physical trauma and ill health

Previous research findings are suggestive of a link between adult physical trauma and the development of rheumatoid arthritis (Al-Allaf et al, 2001), breast cancer (Rigby et al, 2002) and multiple sclerosis (Goodin et al, 1999). Chronic pain has been associated with physically traumatic experiences including surgery (Crombie et al, 1998; Walen et al, 2001; Greenfield et al, 1992; Burckhardt & Jones, 2005), fractures (Castillo et al, 2006; Sanders et al, 2008; Shelat et al, 2012), RTAs (Radanov et al, 2011; Holm et al, 2007; Bortsov et al, 2013; Rosenbloom et al, 2013) and burns (Hamed et al, 2011; Juozapaviciene et al, 2012; Smith et al, 2008). The following section considers in more detail the evidence seeking a direct association between widespread pain and surgery, fractures, RTAs and burns.

c) Adult physical trauma and chronic widespread pain

With regard to widespread pain, a review of the current literature regarding associations with adult physical trauma was carried out using similar search criteria to the review for childhood interpersonal trauma. The search terms were amended to include surgery, fractures, road traffic accidents and burns. Nine studies were identified which have specifically investigated the relationship between adult physical trauma and widespread pain. As shown in Table 2.2, significant associations were found between

widespread pain and surgery in three (60%) studies and RTAs in one (16.7%) study. None of the five studies examining fractures found a significant association with widespread pain. Although burns have been associated with chronic pain (e.g. Smith et al, 2008) no studies were identified assessing the relationship with widespread pain. As was found for childhood interpersonal trauma, validated and reliable measures of CWP / FM were used in all nine studies, but variations were found in the assessment of adult physical trauma, the use of multivariable analysis and the populations studied.

Table 2.2 Associations between widespread pain and adulthood physical trauma

Year	Author	Method	Outcome	Surgery	RTA	Fracture
2002	Al-Allaf et al	Cross-sectional	FM	+	-	-
2005	Broderick & Ross	Cross-sectional	FM	-		
2009	Pamuk et al	Cross-sectional	FM	+		
1999	ter Borg et al	Cross-sectional	FM	+		
1997	Buskila et al	Prospective	FM		+	-
2006a	Wynne-Jones et al	Prospective	WP		-	-
2006	Tishler et al	Prospective	FM		-	-
2011	Tishler et al	Prospective	FM		-	-
2011	Jones et al	Prospective	CWP	-	-	

FM = fibromyalgia; CWP = chronic widespread pain; WP = widespread pain; RTA = road traffic accident; + = significant associations; - = non-significant associations; Empty cells indicate trauma types that were not investigated.

(i) Assessment of adult physical trauma

Cross-sectional studies of patients with FM have found that they report significantly more hysterectomies and appendectomies prior to their diagnosis than rheumatoid arthritis patients (ter Borg et al, 1999; Pamuk et al, 2009). Similarly, Al-Allaf et al (2002) compared the incidence of trauma in FM patients and non-rheumatology patients. The types of trauma examined included surgery, fractures, RTA and work related injuries. The FM patients reported more overall traumatic experiences prior to their diagnosis than the non-rheumatology patients (39% and 7.9% respectively), and specifically more surgeries, but not RTAs or fractures. However, Broderick and Ross (2005) found no difference in the incidence of precursory surgery when comparing FM to rheumatoid arthritis patients.

Five of the studies in Table 2.2 (ter Borg et al, 1999; Pamuk et al, 2009; Al-Allaf et al, 2002; Broderick & Ross, 2005; Jones et al, 2011) used retrospective self-reports of physical trauma. Such self-reports may be subject to recall bias in individuals experiencing the distress and discomfort associated with current pain (Bennett, 2001). Early memory research by Bartlet in the 1930s and Loftus in the 1970s showed the malleability of memory (Schooler et al, 1997). Rather than a direct replay of experienced events, recollections conform to expectations, previous experiences and knowledge. Mood congruent recall refers to the influence of a current emotional state on recall, such that an individual in a negative mood, possibly from the distress of current pain, tends to see their past more negatively (Raphael & Cloitre, 1994). Events are also reinterpreted within current contexts in an effort after meaning (Zaromb & Roediger, 2009), such that individuals with a current illness, such as pain, may focus on negative past experiences in an attempt to attribute a cause to their suffering. For example, recalling events six and 18 months after a traumatic school shooting, individuals with more symptoms at 18 months recalled the incident as more traumatic at 18 months than they did at 6 months, whilst those with fewer symptoms recalled the event as less "harrowing" at 18 months than they did at 6 months (McNally, 2003, pg83). Similarly, by comparing self-reported childhood hospitalisation and operations to those recorded in medical records, McBeth et al (2001c) found that individuals with CWP over reported whilst those with no pain under reported childhood events. This could be seen as evidence of those with CWP seeking a cause for their pain. To assess the extent of such recall bias, the incidence of trauma was objectively confirmed by Al-Allaf et al (2002) with a comparison of 33% of the participants' medical records. 100% concordance was found in 77% of the FM group and 75% of the controls, suggesting that the subjective self-reports were reliable.

Studies using more objective measures of trauma include Buskila et al (1997), Tishler et al (2006, 2011) and Wynne-Jones et al (2006). Both Buskila et al (1997)

and Tishler et al (2006, 2011) compared patients with neck / whiplash injuries to those with fractures. Whilst Buskila et al (1997) found FM in 21.6% of neck injury patients compared to 1.7% of the leg fracture patients three month post-trauma, Tishler et al (2006, 2011) found no such difference. At the first follow up after 12 months, one out of 153 (0.6%) patients suffering whiplash injuries and none of the 53 patients with fractures developed FM (Tishler et al, 2006). At a subsequent follow up after three years, three (2.5%) of those experiencing whiplash and one (3%) with a fracture had developed FM, which is in line with the rates of FM in the general population (Tishler et al, 2011) (see section 1.4.2 pg9). This would suggest no underlying influence on the development of widespread pain from RTAs or fractures.

Adult physical trauma was assessed retrospectively using self-report measures (ter Borg et al, 1999; Pamuk et al, 2009; Al-Allaf et al, 2002; Broderick & Ross, 2005; Jones et al, 2011) and objectively by recruiting participants at the time of the event (Buskila et al, 1997; Tishler et al, 2006 and 2011; Wynne-Jones et al, 2006). A significant association between widespread pain and adult physical trauma was obtained in three (60%) of the studies using self-reports, but only one (24%) of the studies using more objective measures.

(ii) Issues of analysis

Multivariable analysis was used in two of the studies (Jones et al, 2011; Wynne-Jones et al, 2006). Jones et al (2011) obtained pain, sleep and psychological health information at baseline in a community based study. Four years later pain was re-assessed and details obtained of any RTAs, surgeries, hospitalisations and fractures experienced since baseline. The findings of an 84% and 46% increase in the risk of developing CWP for individuals reporting RTAs and fractures respectively were attenuated to non-significant levels when baseline sleep problems and anxiety were taken into account. When examining all the trauma types investigated together, the population attributable risk percentage was 10%, suggesting that eliminating these

trauma types would result in a 10% reduction in the prevalence of widespread pain in the population.

Wynne-Jones et al (2006a) examined the risk of the development of widespread pain in individuals making an insurance claim for an RTA compared to individuals making an insurance claim for a theft or damage to an unoccupied car. At baseline, participants were asked to recall their levels of psychological distress for one month prior to the incident. At six month follow up, 8% of the RTA group and 4% of the non-RTA group had developed widespread pain. The increased risk of the development of widespread pain in the RTA group compared to the non-RTA group failed to reach significance (RR 1.9, 95% CI 0.8 to 4.8). As in the Jones et al (2011) study, the risk was further attenuated (RR 1.4, 95% CI 0.5 to 3.2) when taking account of self-reported psychological distress prior to the insurance claim. It is possible that the distress of the trauma negatively affected responses relating to pre-incident psychological distress, leading to the recall bias discussed above. In both the Wynne-Jones et al (2006a) and Jones et al (2011) studies, psychological stress (including anxiety and sleep problems) in some way explained the relationship between RTAs and widespread pain. The precise nature of the relationship between psychological stress, RTAs and widespread pain could not be identified from the analysis as presented (Jones et al, 2011). However, the trauma diathesis stress model of widespread pain (Section 2.5) specifically examines this relationship, by proposing that traumatic experiences (for example RTAs) create susceptibility, increasing the risk of psychological stress leading to widespread pain.

(iii) Study population

The majority of the participants in the four cross-sectional studies were female patients (Al-Allaf et al, 2002 93%; Broderick & Ross, 2005 98%; Pamuk et al, 2009 100%; ter Borg et al, 1999 100%). Of the prospective studies, only Wynne-Jones et al (2006) and Jones et al (2011) included non-patients. The relationship between

physical trauma in adulthood and widespread pain thus remains relatively unexplored in males and the general population.

In summary, three of the cross-sectional and one of the prospective studies found significant associations between adult physical trauma and widespread pain. However, four prospective studies, those investigating verified events and those accounting for demographic and pre-trauma variables, including psychological stress did not. As with research examining childhood interpersonal trauma, it is proposed that these equivocal findings are the result of the exploration of a direct association between adult physical trauma and widespread pain. Taken together the evidence from the 15 studies (Table 2.1) assessing interpersonal trauma in childhood and the nine studies (Table 2.2) assessing physical trauma in adulthood suggest that where studies employ multivariable analysis techniques to adjust for the potential influence of factors such as psychological stress they are less likely to report an association with widespread pain. The following section therefore examines the evidence of a relationship between psychological stress and widespread pain.

2.3 Psychological stress and widespread pain

The term “stress” has many different definitions and many different meanings (Lucini & Pagani, 2012). This section thus firstly defines what is meant by psychological stress for the purpose of this thesis but presenting evidence from the research literature examining the association between psychological stress (as defined in this study) and widespread pain.

2.3.1 Defining and assessing psychological stress

The term “stress” has been used to describe the cause of stress (the stressor), the evaluation of the stressor, and the resulting effect of that stressor, the physical stress response (Ursin & Eriksen, 2004). Stress can therefore be viewed as a

"system of interdependent processes, including appraisal and coping, which mediate the frequency, intensity, duration, and type of psychological and somatic response" (DeLongis et al, 1988, pg486)

The strength and duration of the physical response to stress thus depends upon the perceived consequences of the event (Lucini & Pagani, 2012) and the individual's perceived ability to cope (Ursin & Eriksen, 2007).

Three different approaches have been taken to investigate the effects of stress; environmental, psychological and biological (Cohen et al, 1995). The environmental approach focuses on the events or experiences that are deemed to be stressful. These include marital or work problems, frustrations, threats and conflict. The subjective experience of life events has been considered during the construction of life event inventories, resulting in the inclusion only of events deemed to be stressful (Brugha et al, 1985). However, there will still be variations in how an individual perceives and reacts to such events (Lazarus, 1990). These factors are consequently included in psychological approaches to the assessment of the effects of stress. The consideration of an individual's level of psychological distress, i.e. levels of anxiety, depression, somatisation and sleep problems, provides useful information with regard to both the individual's interpretation of events and their perceptions regarding their ability to cope (Lazarus, 1990). In order to incorporate these varying aspects of psychological stress, this thesis considers both the occurrence of stressors (environmental) and an individual's level of psychological distress (psychological).

The biological approach

"focuses on activation of specific physiological systems that have been repeatedly shown to be modulated by both psychologically and physically demanding conditions" (Cohen et al, 1995 pg4)

The research evidence of the relationship between widespread pain and the occurrence of stressors (life events), anxiety, depression, somatisation and sleep problems are now considered in turn.

2.3.2 The relationship between widespread pain and life events, anxiety, depression, somatisation and sleep problems

A systematic search was performed of the databases MEDLINE, EMBASE, psychINFO, CINHAL, AMED, BNI and web of knowledge. The search terms included all MESH and thesaurus terms relating to “adult” AND "fibromyalgia" or “fibrositis” or "FM" or "FMS" or "chronic pain" or "chronic widespread pain" or "CWP" or “pain sites” or “sites of pain” or “multi-site pain” AND “psychological stress” or “stress” or “life events” or anxiety or “affective disorders” or depression or “depressive disorders” or “somatisation” or “somatization” or “somatic symptoms” or sleep or insomnia.

The aim of this section was not to present a comprehensive review of all the published data, but rather to provide a summary including exemplars offering evidence for and against the associations between widespread pain and life events, anxiety, depression, somatisation and sleep problems.

a) Life events

A community based cross-sectional study examining the epidemiology of chronic syndromes found that participants reporting two or more significant life events were twice as likely to meet the ACR criteria for CWP as participants reporting no such events (OR 2.2, 95% C.I. 1.9-2.6) (Aggarwal et al, 2006). Similarly, in a four year prospective study, participants reporting no recent life events were twice as likely to remain pain free during the course of the study as participants reporting more than three events (Jones et al, 2009). However, not all studies have shown a significant independent association between life events and widespread pain. For example, in multivariable analysis adjusting for age and sex, participants reporting the occurrence of

two or more life events were not significantly more likely to develop CWP over the course of the study (15 months) than participants reporting no such events (OR 1.2, 95% C.I. 0.9-1.7) (Gupta et al, 2007). As these three community based studies all used the same measure for assessing life events; the List of Threatening Experiences (Brugha et al, 1985), the difference in findings cannot be explained by the inclusion of different events. However, as described above, the significance of these events may vary between individuals. The association with widespread pain may therefore be related to the detrimental effects these events have, rather than their occurrence per se. Considering these events in combination with measures of psychological distress may therefore assist in elucidating any relationship.

b) Anxiety

Anxiety is the concern regarding some possible future threat or worry generalised to a number of events (Leeuw et al, 2007; Andrews et al, 2010; Estes & Skinner, 1941). This results in physiological hyperarousal, including feelings of tension and agitation (Antony et al, 1998). Anxiety has been associated with widespread pain in both cross-sectional and prospective studies. For example, in a community based study including 85,088 participants from 17 European countries, Gureje et al (2008) examined the prevalence of anxiety disorders including generalised anxiety disorder, panic disorder, post-traumatic stress disorder and social phobias. As with the Kamaleri et al (2008a) study described in Section 1.4.3 pg14, the prevalence of anxiety disorders increased with the number of pain sites. Compared to individuals without pain, those with pain in a single site and those with pain in two or more sites, were twice and four times more likely to have an anxiety disorder, respectively (Gureje et al, 2008). Anxiety has also been associated with the persistence of CWP. In a community based prospective study, individuals whose CWP persisted at 15 month follow up had higher levels of anxiety at baseline than those who no longer met the ACR criteria (Davies et al, 2008).

c) Depression

Depression is typically characterised by low levels of emotional arousal (Moratti et al, 2008). Symptoms include dysphoric mood and the loss of self-esteem, incentive and expectations about the future (Lovibond & Lovibond, 1995; Antony et al, 1998). Cross-sectionally, Aggarwal et al (2006) found the prevalence of probable depressive disorder to be 13% in individuals with CWP, compared to 2% in those without the condition. Depression has also been associated with the development of widespread pain in prospective studies. Holm et al (2007) followed 266 traffic injury claimants with localised neck and back pain for 12 months. Over the course of the study, 56 (21%) participants developed widespread pain (assessed as pain in greater than 9 sites out of 45). The risk of the development of widespread pain was three times higher in those participants with depression at baseline (OR 3.2, 95% C.I. 1.6-6.3). Depression has also been associated with CWP persistence (Davies et al, 2008). However, one study (Kindler et al, 2010), found that depression did not predict the transition from chronic neck or chronic back pain to CWP over six years. It is plausible that depression had no predictive ability in the Kindler et al (2010) study because a validated measure of depression was not used. Kindler et al (2010) examined the presence or absence of nine symptoms of depression experience two weeks prior to baseline, whilst Holm et al (2007) used the Center for Epidemiological Studies Depression Scale, a valid and reliable instrument (Blalock et al, 1989). The period of follow-up also differed between the two studies. The predictive ability of depression was assessed after six years by Kindler et al (2010) and one year by Holms et al (2007). However, Forseth et al (1999) did find that depression predicted the development of FM in female patients with back pain, using a self report of depression and over a five year period.

d) Somatisation

Somatisation is the process by which emotions are expressed as bodily symptoms (McWhinney & Epstein, 1997). Common symptoms associated with somatisation typically include nausea, vomiting and troubles with vision. Such symptoms are said to

reflect “psychological distress” (Derogatis & Melisaratos, 1983, pg596). Somatisation has been associated with both CWP development and persistence. For example, in two community studies, the risk of CWP development at 12 month follow up was significantly increased (OR 3.3, 95% C.I. 1.5 – 7.4) in participants reporting three or more somatic symptoms at baseline (McBeth et al, 2001a), and age and somatic symptoms were associated with CWP persistence over 7 years (Papageorgiou et al, 2002).

e) Sleep

Sleep problems affect cognitive functioning and mood and can lead to and result from allostatic load (McEwen, 2006). Poor quality sleep affects between 40% and 90% of CWP patients (Silverman et al, 2010). Problems include short sleep duration with frequent awakenings and periodic limb movements (Lavigne et al, 2011). Studies using electroencephalography have shown alterations in sleep patterns in CWP patients when compared to healthy controls. These alterations include reduced slow wave delta sleep (Okura et al, 2008) and increased fast frequency alpha sleep; with alpha intruding on delta activity (the alpha-delta sleep anomaly) during non-rapid eye movement sleep (Lavigne et al, 2011; Moldofsky, 2008). These reductions in slow wave sleep detrimentally affect endocrine, metabolic (Huber, 2009) and immune functioning (Besedovsky et al, 2012).

It could be argued that sleep is disrupted by pain. A longitudinal study of 333 major burn victims shows the reciprocal interactive between pain and insomnia. Sleep onset insomnia prior to discharge from a burns centre significantly predicted the severity of bodily pain at 6, 12 and 24 month follow up, when controlling for discharge pain severity. Similarly discharge pain severity and pre-burn psychological distress (anxiety and depression) significantly predicted sleep onset insomnia at follow up when controlling for discharge insomnia (Smith et al, 2008). However, prospective studies have shown that self reported poor sleep increases the risk of CWP and FM

development (Gupta et al 2007; Mork & Nilsen, 2012) and that sleep quality predicts later pain in FM patients (Bigatti et al, 2008). Furthermore, artificially induced alpha-delta sleep has been shown to produce widespread pain type symptoms in healthy individuals (Moldofsky, 2008), whilst restorative sleep has been associated with the resolution of CWP (Davies et al, 2008).

f) Life event, anxiety, depression, somatisation and sleep problems combined

Life events, anxiety, depression, somatisation and sleep problems have all been associated with the development and persistence of CWP individually. Functional impairment is, however, more strongly associated with these factors when they are considered in combination (Lowe et al, 2008). For example, in a community based prospective study, Gupta et al (2007) found that anxiety, depression, somatisation, sleep problems and life threatening events increased the risk of CWP development at 15 month follow-up. In particular, individuals with high levels of illness behaviours, somatisation and sleep problems were 12 times more likely to develop CWP than those with low levels of these three factors (OR 12.1 95% CI 5.9, 24.7).

The relationship between life events, anxiety, depression, somatisation and sleep problems is complex, with considerable correlations and comorbidity between them (Lovibond & Lovibond, 1995; Antony et al, 1998; Akerstedt et al, 2012; Burton et al, 2009; Rosmalen et al, 2012). Individuals experiencing psychological distress may perceive life events as more negative (Sandin et al, 2004), whilst anxiety, depression, somatisation and sleep problems may be indicative of negative reactions to such life events (Specchio et al, 2004; Sandin et al, 2004; Brugha et al, 1985). It is therefore proposed that the examination of the occurrence of recent life events, in combination with levels of anxiety, depression, somatisation and sleep problems, provides a better reflection of an individual's phenomenological experience of psychological stress, than by considering these factors individually.

This section examined the research evidence of the relationship between psychological stress and widespread pain. For the purpose of this thesis, psychological stress is defined by the combination of life events and anxiety, depression, somatisation and sleep problems. In the research evidence presented psychological stress, in the form of life events, anxiety, depression, somatisation and sleep problems was consistently and robustly associated with widespread pain (Jones et al, 2009; Davies et al, 2008; Holm et al, 2007; Papergeorgiou et al, 2002; Mark & Nilsen, 2012; Gupta et al, 2007). However, not everyone who experiences psychological stress goes on to develop widespread pain. For example, only 16% and 17% of a community sample of individuals with probable anxiety and depressive disorders respectively, went on to develop CWP at 15 month follow up (Gupta et al, 2007). This suggests that some individuals may be more susceptible than others to the development of widespread when they are stressed. Two potential causes of such susceptibility (diathesis) are proposed: trauma and sex. The following section examines the concept of diathesis and theoretical models examining the relationship between trauma and widespread pain.

2.4 Theoretical models of trauma and widespread pain

2.4.1 Diathesis stress models

The term diathesis refers to an underlying biological, psychological or social susceptibility that predisposes an individual towards psychological and / or physical ill health (Ingram & Luxton, 2005). Individual susceptibilities have long been implicated in the development of illness; the concept of diathesis being the basis of Hippocrates' four humors theory of disease (Monroe & Simons, 1991). The influence of stress was recognised as an important factor in psychological disorders in the 19th century (Bucknill & Tuke, 1858) and in physical disorders following the work of Selye in the 1950s (Selye, 1984). The two concepts, diathesis and stress, were then considered together in work examining the aetiology of schizophrenia, when it was recognised that not everyone experiencing stress went on to develop the condition (Bleuler, 1963). The diathesis stress framework has subsequently been applied to the development of other psychiatric

disorders, including depression (Hankin & Abramson, 2001), anxiety (Chorpita & Barlow, 1998) and phobias (Kendler et al, 2002); and has also been applied to physical ill-health (Peterson et al, 1988; Jackson et al, 2002).

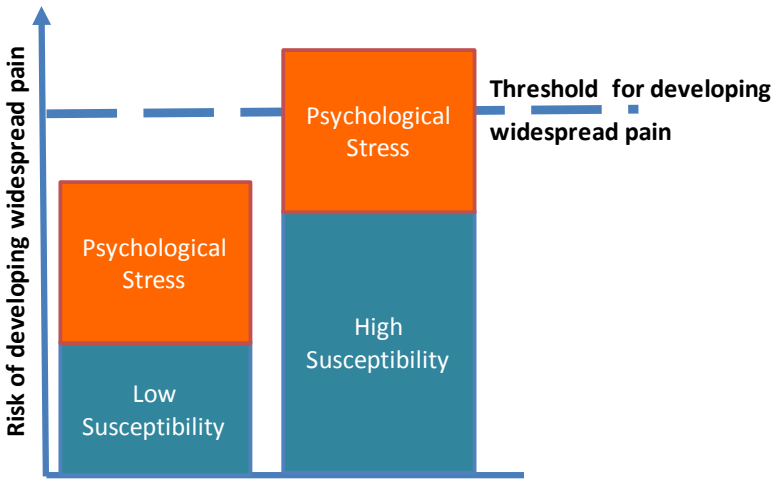
How do diathesis stress models explain the development of chronic pain?

"The basic premise is that stress activates a diathesis, transforming the potential of predisposition into the presence of psychopathology."

(Monroe & Simons, 1991, pg2)

Diathesis stress models propose that the presence of a diathesis or susceptibility is not sufficient for the development of a disorder (Ingram & Luxton, 2005). The underlying susceptibility is only activated by stress. Thus an individual's risk of developing widespread pain depends upon both their pre-existing susceptibility and their current level of stress. As shown in Figure 2.1, a highly susceptible individual reaches the threshold for widespread pain, even when experiencing a similar level of stress that does not cause the disorder in an individual with low susceptibility. A much higher level of stress is required for an individual with low susceptibility to reach this threshold.

Figure 2.1 Relationship between susceptibility and stress



Source: Original

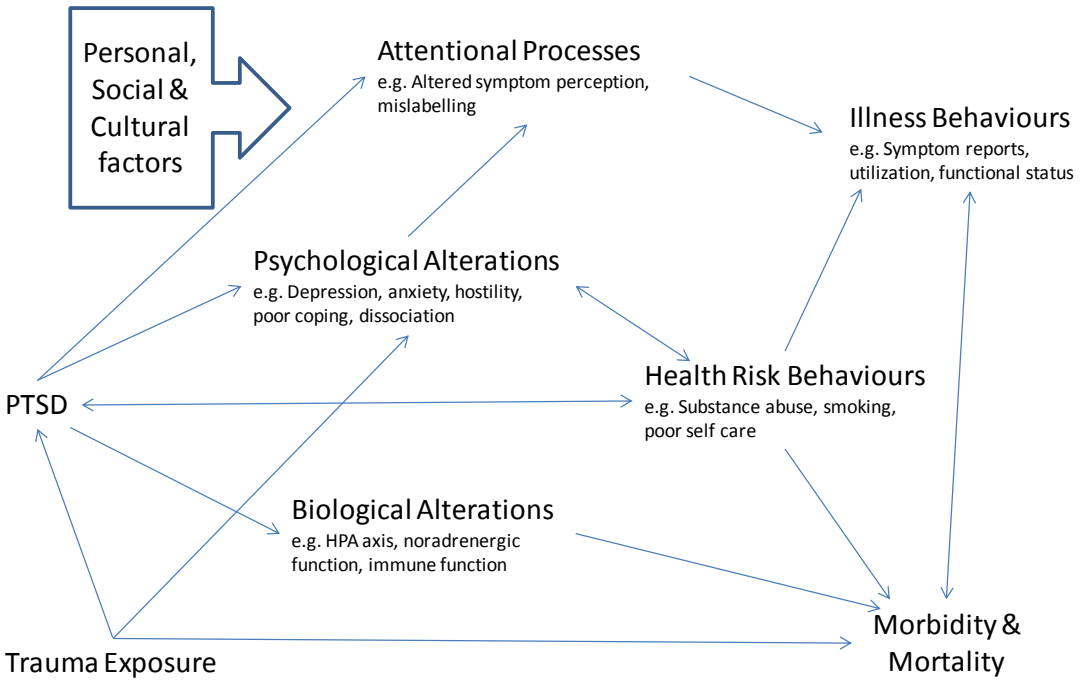
With regard to chronic pain conditions, five diathesis stress models have been identified. Dworkins and Banks' (1999) model examines the development of postherpetic neuralgia pain. The models of Turk (2002), Meredith et al (2008) and Hamilton et al (2012) are primarily concerned with the adjustment to, rather than the development of chronic pain conditions. The diatheses in these models are anxiety sensitivity, insecure attachment and sleep problems, respectively. Although Okijuki and Turk's (1999) diathesis stress model does examine the development of FM, the diatheses in this model are biological and psychosocial factors, rather than traumatic experiences.

Traumatic experiences have been implicated as a diathesis for the development of post-traumatic stress disorder (PTSD) (McKeever & Huff, 2003) and have been posited as a risk factor for the development of widespread pain (Van Houdenhove et al, 2001, 2004; Kendall-Tackett & Klest, 2009). However, no diathesis stress model has been identified to date, which specifically considers traumatic experiences as a diathesis for widespread pain.

2.4.2 A model of trauma exposure and physical health

One model that does consider traumatic experiences, although not as a diathesis, is Schnurr and Green's (2004a) model of trauma exposure and physical health. In their model, PTSD is proposed as a mediator by which trauma leads to ill health, as shown in Figure 2.2. PTSD is a trauma and stress related disorder characterised by symptoms of re-experiencing (intrusive thoughts or recurrent dreams of the event); avoidance of thoughts, feelings and reminders of the event; negative cognitions and mood (including distorted blaming of self or others) and arousal (aggressive, reckless or self-destructive behaviour, sleep disturbances or hypervigilance) (Diagnostic and Statistical Manual [DSM] fifth edition, 2013).

Figure 2.2 A model of trauma exposure and physical health



Source: Schnurr and Green (2004a), based on the model of Physical Health and PTSD by Schnurr and Jankowski (1999)

This model proposes that the distress reactions of PTSD resulting from traumatic experiences lead to biological changes in the stress and immune systems. Both trauma exposure and PTSD then lead to psychological alterations and changes in attentional processing. For example, the use of the defence mechanism of dissociation can then lead to altered symptom perception and to illness behaviours such as increased symptom reporting and health care utilisation. Health risk behaviours may then result from other psychological factors. For example, maladaptive coping may lead to self-medication, where the individual uses alcohol or tobacco to provide short term relief from negative affect (Anda et al, 2006). The model also recognises the influence of personal, social and cultural factors in the development of ill health. These include genetics, personality, age, sex and socioeconomic status as well as cultural and ethnic differences.

This comprehensive model provides clear directionality whilst maintaining the complex interactions between its components. Each of the individual components may be insufficient for ill health on their own. It is the cumulative and interactive effects of the

biological, psychological and behavioural alterations that lead to physical health problems (Schnurr & Green, 2004a). Schnurr and Green's (2004a) model

"suggests that PTSD plays a crucial role in mediating the relationship between traumatic exposure and poor physical health" (Schnurr & Green, 2004b, pg7)

The authors also recognise that other stress or distress reactions may be sufficient. Individuals may experience considerable trauma related distress without meeting the specific criteria for PTSD (Briere & Spinazzola, 2005; Ruscio et al, 2002). Schnurr and Green's (2004a) model is of particular relevance to the current study as it combines the effects of both trauma and psychological stress in the development of physical ill health.

Other theories that specifically incorporate traumatic experiences, including Brown's (2004) integrative conceptual model of medically unexplained symptoms and the model of somatoform symptoms (Kirmayer & Young, 1998) are discussed briefly below (see Section 2.5.2). Unlike Schnurr and Green's (2004a) model, these models contain multiple components with multi-directional interactions, and whilst this may reflect the complex aetiology of widespread pain, the models are not easily testable. However, as with Schnurr and Green's (2004a) model, these models do not consider traumatic experiences as a diathesis.

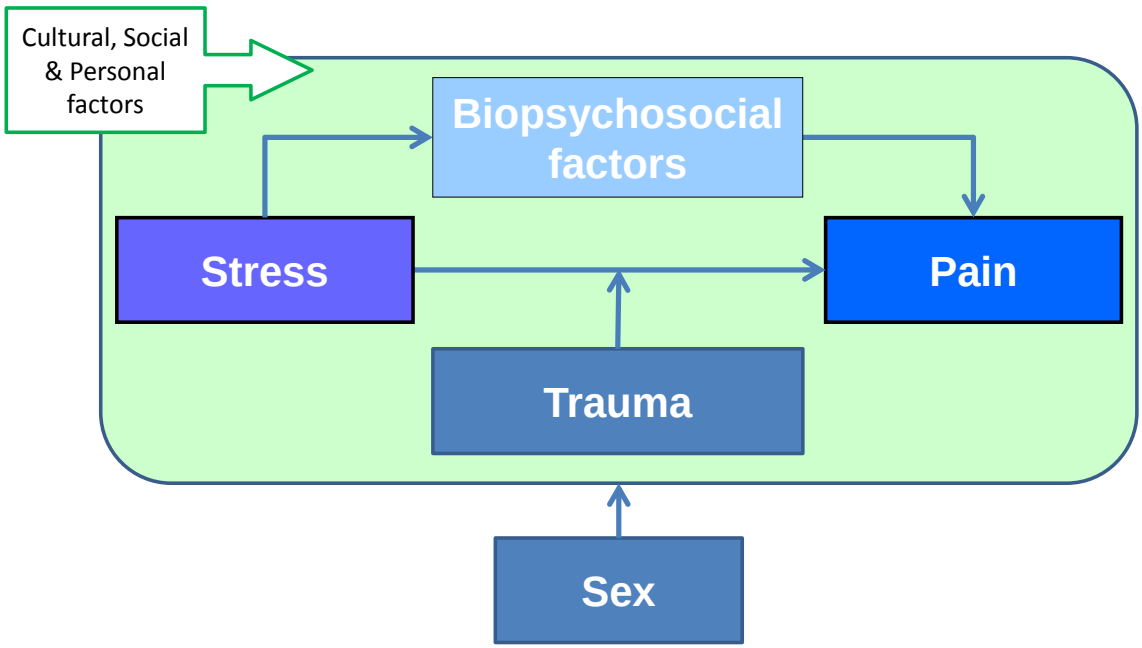
In the study by Raphael et al (2011) described in Section 2.2.2b, contrary to the predictions of the Schnurr and Green (2004a) model, PTSD did not mediate the relationship between childhood abuse and pain. The findings of this study suggest that the traumatic experience of childhood abuse was insufficient to trigger the development of pain symptoms on its own. An interaction of childhood abuse and PTSD was required for the development of pain symptoms and pain problems. The presence of PTSD may be a reflection of the severity and detrimental impact of the abuse (Brewin et al, 2000) or the abuse may have increased susceptibility to the development of PTSD in response to subsequent stressors (McKeever et al, 2003). These findings, when considered with

those from the Jones et al (2011) and Wynne-Jones et al (2006) studies (described in Section 2.2.3.c), are more suggestive of trauma as a susceptibility factor, increasing the subsequent risk of widespread pain when an individual is exposed to psychological stress. It would be more appropriate, therefore, to consider these factors within a diathesis stress framework. As no relevant diathesis stress model which explains the relationship between trauma, stress and widespread pain could be identified, the trauma diathesis stress model of widespread pain was developed.

2.5 Trauma diathesis stress model of widespread pain

The trauma diathesis stress model, shown in Figure 2.3, proposes a direct association between psychological stress and widespread pain, which is mediated by biological, psychological and social factors and moderated by traumatic experiences and sex. The model also recognises that widespread pain can be affected by cultural, social and personal factors (Kirmayer et al, 2004).

Figure 2.3 Trauma diathesis stress model of widespread pain



Source: original

It is proposed that exposure to trauma creates a susceptibility (diathesis), which increases the risk of developing widespread pain when an individual is exposed to psychological stress. The model also proposes that the effects of trauma and its

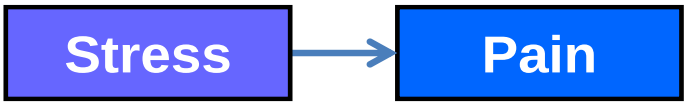
relationship to widespread pain are different for males and females. Psychological stress may reactivate the effects of prior trauma, triggering for example dissociation (van der Kolk et al, 2007a) or insecure attachment styles (Meredith et al, 2008); or may apply additional pressure to the stress, immune and pain processing systems already weakened by the prior exposure to trauma. The diatheses examined in this study are childhood abuse and adult physical trauma. As described below, psychological and physical traumatic experiences can initiate long term psychological and physiological changes in an individual, thus creating a diathesis.

The trauma diathesis stress model of widespread pain extends prior work by Schnurr and Green (2004a) by setting their trauma exposure and physical health model into a diathesis stress framework. However, the trauma diathesis stress model of widespread pain differs from Schnurr and Green's model in that it accounts for the fact that traumatic experiences are not essential to the development of widespread pain. Research is presented above which demonstrates that psychological stress can lead to widespread pain without the previous experience of a trauma. And yet not everyone who experiences stress goes on to develop widespread pain. In light of this, the trauma diathesis stress model of widespread pain examines who is susceptible to developing widespread pain when stressed; i.e. whether exposure to trauma moderates the relationship between psychological stress and widespread pain (hereafter referred to as the stress pain relationship). Each element of the trauma diathesis stress model of widespread pain is examined in more detail below.

2.5.1 Direct relationship: Psychological stress and widespread pain

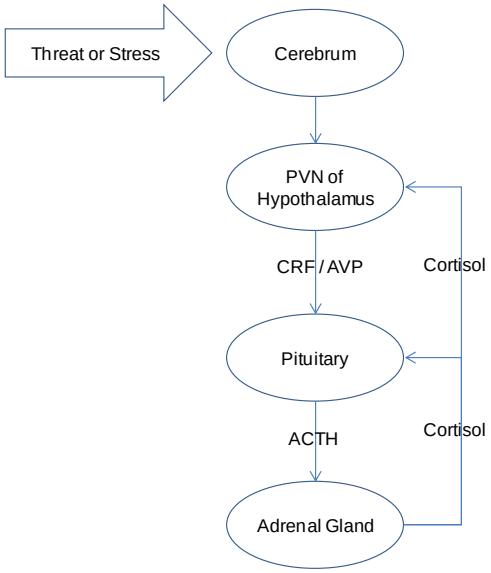
The first part of the trauma diathesis stress model proposes that psychological stress leads directly to widespread pain, as shown in Figure 2.4. In order to demonstrate how stress can lead to widespread pain, this section presents a description of the physiological response to stress.

Figure 2.4 Trauma diathesis stress model – Stress and pain



Selye described stress as a “nonspecific response of the body to any demand” (1984, pg472). As such, stress can be viewed as an adaptive response, involving physiological, psychological and behavioural changes aimed at maintaining stability (homeostasis). The stress response involves a cascade of autonomic, endocrine and immune system responses triggered by physical or psychological stress and inflammatory processes (Olson et al, 2011). The sympathetic nervous system is activated, causing an increase in respiration and heart rate and the inhibition of digestion, as blood flow is diverted to the muscles in preparation for dealing with an emergency. The hypothalamus controls endocrine function and provides inputs to the brain stem to coordinate autonomic regulation (Lovallo, 2005). As shown in Figure 2.5, when a threat is encountered, information from the cerebrum triggers the hypothalamic-pituitary-adrenal (HPA) axis; the primary stress pathway. This is activated by the release of corticotrophin-releasing factor (CRF) and arginine vasopressin (AVP) in the paraventricular nucleus (PVN) of the hypothalamus. CRF and AVP act on the pituitary, stimulating the production of adrenocorticotropic hormone (ACTH), resulting in the production and release of cortisol from the adrenal gland. Further release of CRF and ACTH is inhibited directly by the feedback of cortisol to the pituitary gland, hypothalamus, and other brain areas and indirectly by substance P (via gamma-aminobutyric acid (GABA) and serotonin in the PVN), halting the stress response when the threat is resolved (Gillespie & Nemeroff, 2007; Carrasco & Van der Kar, 2003).

Figure 2.5 Hypothalamic-pituitary-adrenal axis



Adapted from Gillespie & Nemeroff, 2007

When faced with a challenge the body adapts to achieve homeostasis. However, if the challenge is not met or neutralised, the cost of maintaining homeostasis in the face of continuing challenges can lead to allostatic load and long term dysregulation of the system (McEwen, 1998). This increases sensitivity to subsequent stressors (Friedman & McEwen, 2004) and changes the perception of pain (McEwen, 1998). Resulting alterations in the functioning of the HPA axis can lead to insufficient or excessive secretion of CRF, ACTH and cortisol (Pruessner et al, 1999). In support of this, cross-sectional studies have found cortisol levels to be directly related to pain symptoms in FM patients (McLean et al, 2005a), and prospective studies have shown that HPA axis dysregulation significantly increases the risk of new-onset CWP (McBeth et al, 2007).

Other effects of the physical stress response include alterations in endocrine function. Depleted levels of serotonin and norepinephrine, which reduce the descending inhibition of pain (Fishbain et al, 1997), have also been implicated in the development of anxiety, depression, somatisation and sleep problems (Chou et al, 2012; Goddard et al, 2010; Popa et al, 2008; Ebner & Singewald, 2006). Clearly there is a link between the physiological changes associated with the stress response and symptoms such as

anxiety, depression, somatisation and sleep problems. The physical stress response thus provides a plausible physiological process by which stress can lead to pain.

2.5.2 Mediators of the stress pain relationship

The second part of the trauma diathesis stress model explores the potential biopsychosocial mediators of the stress pain relationship. A mediator is a factor that clarifies how or why a relationship exists between two variables. In order to explain how stress might lead to pain, a potential mediator must be associated with both stress and pain. This section examines the research evidence for potential mediators of the stress pain relationship in each of the biological, psychological and social domains.

a) Biological mediators of the stress pain relationship

Biological factors proposed to mediate the stress pain relationship include peripheral abnormalities, central sensitisation and genetics.

(i) Peripheral abnormalities

One proposed mechanism for widespread pain is that the pain originates from structural, metabolic and microcirculatory abnormalities within the muscles (Stein et al, 2009). Cellular damage and mitochondrial abnormalities have been found in FM patients in support of this (Bengtsson, 2002; Sprott et al, 2000). Reduced blood flow and oxygenisation have also been observed in muscles and the skin overlying tender points in FM patients (Jeschonneck et al, 2000). It has been proposed that the reduced blood flow leads to the accumulation of metabolites and hypoxia which leads to pain, reduced endurance and premature exhaustion (Lund et al, 2003; Gerdle et al, 2010). These findings may explain why individuals with widespread pain experience a lack of muscle strength and reduced physical endurance, with elevated pain levels during and following exercise (Bengtsson, 2002). However, muscle mitochondria and histochemistry are dependent upon activity levels (Holloszy et al, 1984) and studies comparing FM patients and sedentary controls have found no difference in muscle

energy metabolism (Simms et al, 1994). So the changes seen in widespread pain patients may be a consequence of deconditioning rather than the cause of widespread pain (Abeles et al, 2007). No definitive muscle pathology has so far been associated with widespread pain and considered on their own, such peripheral abnormalities fail to address the cluster of additional symptoms associated with widespread pain, for example sleep and cognitive disturbances. However, continued nociceptive input from peripheral abnormalities can lead to central sensitisation (Voscopoulos & Lema, 2010).

(ii) Central Sensitisation

Central sensitisation results in functional changes within the central nervous system leading to heightened pain perception (Voscopoulos & Lema, 2010). The continued stimulation of the pain and stress systems or persistent inflammation (Voscopoulos & Lema, 2010; Lyon et al, 2011) lead to an excess of glutamate, substance P, prostaglandins and cytokines (Voscopoulos & Lema, 2010) and a depletion of the pain inhibiting neurotransmitters serotonin, norepinephrine, and dopamine (Yunus, 2008). The subsequent alterations to cell connectivity and excitability result in the under activity of descending inhibitory and over activity of ascending and descending facilitatory pathways, increasing overall nociceptive transmission (Nijs et al, 2011). These changes reduce pain thresholds (hyperalgesia), widen the receptive field (referred pain or secondary hyperalgesia) and alter the perception of previously innocuous stimuli such that they are experienced as painful (allodynia) (Voscopoulos & Lema, 2010). In support of this, research using animal models has shown that tissue injury at a single site can result in long term increased pain sensitivity throughout the body (Wang et al 2004). Once the system has been sensitised, peripheral pathology and noxious stimuli are no longer necessary for pain to be experienced (Latremoliere & Woolf, 2009).

"In this sense central sensitization represents an uncoupling of the clear stimulus response relationship that defines nociceptive pain." (Woolf, 2011, pg4)

Central sensitisation offers a viable explanation for widespread pain, as sufferers experience hyperalgesia, secondary hyperalgesia and allodynia (Staud et al, 2012; Meeus & Nijs, 2007; Kindler et al, 2011). Increased levels of substance P, diffuse noxious inhibitory control dysfunctions, disruption to the release of dopamine in the basal ganglia, and decreased mu-opiate binding have also been found in FM patients (Apkarian et al, 2009). However, central sensitisation cannot account for the co-morbid cognitive impairment associated with widespread pain (Lyon et al, 2011). Central sensitisation has also been implicated in many conditions co-morbid with widespread pain, including chronic fatigue, headache and irritable bowel (Yunus, 2007; Meeus et al, 2009). Central sensitisation may be seen as an explanation of pain persistence rather than as an aetiological factor. However, early experiences of pain, particularly during the critical period of the first post-natal week for rat pups, can significantly alter the development of the pain processing system (Walker et al, 2009a). Similarly children who experienced numerous early surgical procedures due to prematurity have been found to have more widespread activation of cortical neurons in response to pain and altered pain sensitivity compared to age-matched healthy controls (Slater et al, 2010; Walker et al, 2009b). This suggests that functional changes occurring early during development may later be triggered, possibly by stress, without the necessity of further nociceptive input. There may also be a genetic component to susceptibility to central sensitisation (Woolf, 2011).

(iii) Genetics

Strong familial aggregation (Arnold et al, 2004) and twin studies (Kato et al, 2006) suggest a genetic, heritable component to widespread pain. Evidence from twin studies suggest heritability estimates of between 48-54% (Kato et al, 2006) for CWP. Genetic factors have been associated with experimental pain sensitivity (Norbury et al, 2007; Diatchenko et al, 2005), the synthesis and metabolism of enzymes and proteins within the pain processing system, recovery from injury (Singer & Clark, 1999) and the

efficacy of analgesic drugs in cancer pain (Reyes-Gibby et al, 2007). A number of potential candidates for widespread pain have been identified. Mutations in the *SCN9A* gene have been found to cause congenital insensitivity to pain (Indo et al, 1996). The serotonin transporter gene (Offenbaecher et al, 1999) and the dopamine receptor gene (Buskila & Sarzi-Puttini, 2006), both of which have been implicated in a susceptibility to stress and affective disorders, are associated with the descending inhibition of pain (Van Houdenhove & Egle, 2004). Catecholamine-O-methyltransferase (COMT) haplotypes have been associated with pain sensitivity (Diatchenko et al, 2005) but not CWP (Hocking et al, 2010). However, it is difficult to distinguish genetic variations that are specifically associated with pain from psychological and environmental confounders, making this research particularly challenging (Limer et al, 2008).

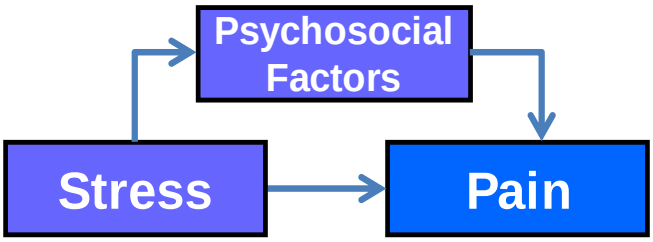
There are clear biological mediators involved in the experience of pain. Peripheral abnormalities may lead to central sensitisation, resulting in the heightened perception of pain. These mediators may also be affected by psychological stress. For example, allostatic load can disrupt muscle and tissue repair (Friedman & McEwen, 2004), whilst elevated levels of substance P, indicative of an unresolved stress response, also implicate the stress system in the development of central sensitisation (Lyon et al, 2011). Genetic factors may moderate the stress pain relationship, increasing an individual's susceptibility to the development of widespread pain (Dworkins & Banks, 1999), or may mediate the relationship, as psychological stress has also been shown to alter the expression of genes (Li et al, 2013). Although peripheral abnormalities, central sensitisation and genetic factors may mediate the stress pain relationship, this thesis focuses on the potential psychological and social mediators described below.

b) Psychological mediators of the stress pain relationship

The experience of pain is not just a direct sensory or stimulus-response to noxious stimuli. Emotions, cognitions and perceptions all influence and are influenced by the

pain processing system. A systematic search was performed, building on the search criteria used for the assessment of a relationship between psychological stress and widespread pain (detailed in Section 2.3.2). Additionally all MESH and thesaurus terms relating to "dissociation" or "dissociative experiences" or "health anxiety" or "somatosensory amplification" or "personal control" or "mastery" or "locus of control" were included. The search criteria where expanded to include an outcome of general physical health in order to provide further information with regard to the potential mediating effects of these factors, particularly where direct evidence of their association with psychological stress and widespread pain was unavailable. By describing the psychodynamic and cognitive behavioural theories of widespread pain and providing exemplars of the research evidence, this section demonstrates how dissociation, health anxiety, somatosensory amplification and personal control have the potential to mediate the stress pain relationship (Figure 2.6).

Figure 2.6 Trauma diathesis stress model – Psychosocial mediators



(i) Dissociation

Psychodynamic theories of chronic pain include the conversion of underlying emotional conflicts into physical symptoms (Weisberg & Keefe, 1999) and dissociation. Dissociation is defined as disruptions in the normal integration of memories, perceptions and identity as an emotional response to trauma (Van Der Hart & Horst, 1989). During the course of a traumatic event a person may experience an altered state of consciousness, in which they find themselves detached from the experience, their body, their sense of self and / or the external world (Holmes et al, 2005). Once used, this defence mechanism can then be triggered by stress in everyday contexts

(Spiegel et al, 2011). Whilst dissociation offers protection from the immediate overwhelming emotional effects of trauma, in the long term the lack of integration of experiences can lead to confusion between external and internal, psychological and physical sensations (Bob, 2008). This may lead to a misinterpretation of sensations and also to the abnormal activation of the pain processing system (Bob, 2008). Although this model is essentially cognitive in focus (Rief & Broadbent, 2007), Brown's (2004) integrative conceptual model of medically unexplained symptoms includes the concept of dissociation. This model proposes that incoming stimuli may be misinterpreted and incorrectly associated with rogue representations. These rogue representations are memories that have been acquired directly, from our own previous experiences of illness and pain or indirectly from the observation of physical symptoms in others. They are also shaped by exposure to general information from the cultural / social environment (Brown, 2004).

Dissociation has also been associated with depression and anxiety in a non-clinical community based study (Levin & Spei, 2004) and with somatisation in chronic pelvic pain patients (Badura et al, 1997). Dissociation can result in altered pain sensitivity (Horowitz & Telch, 2007; Fillingim & Edwards, 2005) and reduced pain thresholds (Agargun et al, 1998). FM patients have been found to score more highly on measures of dissociation than patients with rheumatoid arthritis (Naring et al, 2007; Leavitt & Katz, 2003; Walker et al, 1997). Dissociation has been associated with both psychological stress and widespread pain. The trauma diathesis stress model of widespread pain therefore proposes that psychological stress leads to the inappropriate resurfacing of dissociated experiences relating to previous pain, resulting in the experience of widespread pain.

(ii) Health anxiety and somatosensory amplification

Cognitive behavioural theories of pain focus on the role of disturbed perceptions and cognitions. As well as Brown's integrative conceptual model of medically

unexplained symptoms (Brown, 2004), other models include the circle of somatosensory amplification (Barsky & Wyshak, 1990), the model of somatoform symptoms (Kirmayer & Young, 1998) and the perception-filter model of somatoform disorders (Rief & Broadbent, 2007). Whilst varying in focus, complexity and terminology all emphasise the roles of health anxiety and somatosensory amplification in the development of physical ill health.

Health anxiety involves the worry about illness based on dysfunctional assumptions and beliefs (Marcus & Church, 2003). Health anxiety is characterised by a fear of disease and the conviction of the presence of a disease, a belief which is resistant to reassurances from others, including medical professionals (Pilowsky, 1967). Somatosensory amplification refers to the enhancement of normal physiological sensations resulting from heightened awareness. Barsky and Wyshak's (1990) circle of somatosensory amplification describes how individuals can become trapped within a perpetuating cycle, whereby anxiety regarding health leads to a focus on physical sensations. Due to this focus, normal bodily sensations are amplified and misinterpreted as relating to illness and disease. This leads to further health anxiety and attention being focused on the body, which further amplifies the perception and misattribution of physical sensations.

The physical symptoms associated with psychological stress, such as accelerated heart rate and increased sweating, may trigger health anxiety and / or somatosensory amplification leading to an increase in pain. Anxiety, depression and somatisation have been associated with both health anxiety and somatosensory amplification in cross-sectional studies (Barsky et al, 1988; Hanel et al, 2009). Psychological stress has also been associated with later health anxiety in prospective studies (Barsky et al, 1998; Olatunji et al, 2009). For example, Barsky et al (1998) assessed patients for hypochondriasis, an extreme form of health anxiety, using a structured diagnostic interview. At four year follow up, those individuals who still met the diagnostic criteria

for hypochondriasis had significantly higher levels of somatisation at baseline than those whose hypochondriasis had remitted. In a non-clinical population, Olatunji et al (2009) found a significant correlation between stress at baseline and health anxiety at 12 week follow-up. High levels of health anxiety and somatosensory amplification have been associated with myofascial face pain (Raphael et al, 2000), irritable bowel syndrome and CWP (Aggarwal et al, 2006; Geisser et al, 2008; Sayar et al, 2005; Epstein et al, 1999). Although health anxiety has been significantly associated with CWP in cross-sectional studies (for example Aggarwal et al, 2006), in prospective studies health anxiety has not predicted the development or persistence of CWP over twelve months (McBeth et al, 2001a&b). This difference may indicate that health anxiety is a consequence rather than a cause of CWP or may be due to the way health anxiety was measured. Aggarwal et al (2006) used the Health Anxiety Questionnaire (Lucock et al, 1996), whilst McBeth et al (2001a&b) used the health anxiety subscale of The Illness Attitude Scales (Kellner et al, 1987). Alternatively, the relationship between health anxiety and CWP may be more complex. The trauma diathesis stress model of widespread pain therefore proposes that the physical symptoms of psychological stress may lead to heightened concern regarding one's health, resulting in a misinterpretation of amplified bodily processes which in turn lead to the experience of widespread pain.

(iii) Personal control

Personal control, or mastery,

"refers to the extent to which people see themselves as being in control of the forces that importantly affect their lives" (Pearlin et al, 1981, pg340)

High levels of personal control are associated with adherence to treatment (Weinman et al, 1996), reduced levels of depression and interference of pain in daily life following treatment for CWP (de Rooij et al, 2013), and the use of adaptive coping strategies, resulting in more positive health outcomes (Hagger & Orbell, 2003). In

support of this, low levels of personal control have been associated with increased pain and reduced physical functioning in FM patients (Stuifbergen et al, 2006).

Whilst high levels of personal control can increase resilience against the effects of stress (Neupert et al, 2007; Diehl & Hay, 2010), high levels of stress can also reduce an individual's sense of personal control (Glavin, 2013). In a study by Price et al (2002), personal control was found to mediate the relationship between stress (the financial strain caused by job loss) and poor health. The uncontrollability of a stressor has also been associated with a greater cortisol response (Dickerson & Kemeny, 2004). Personal control has thus been associated with psychological stress (Price et al, 2002). Although no studies were identified which examined the role of personal control in the development of widespread pain, research suggests that low levels of personal control may have a detrimental effect on pain that is already present (Stuifbergen et al, 2006). The trauma diathesis stress model of widespread pain therefore proposes that psychological stress leads to a reduced sense of personal control which results in an increase in the widespreadness of pain by reducing the use of effective coping strategies and treatment adherence.

In summary, psychological stress can trigger positive dissociative symptoms, heighten concern regarding one's health, focus attention on physiological processes and lead to a reduced sense of personal control. These alterations brought about by stress could lead to rogue representations, a misinterpretation of amplified bodily processes and maladaptive coping strategies. These components then increase the likelihood of the subsequent development of widespread pain

c) Social mediators of the stress pain relationship

In addition to biological and psychological factors outlined above, social factors such as social support and adult attachment style are also proposed as mediators of the stress pain relationship. The search terms used in Section 2.5.2b were amended to

examine associations between psychological stress, widespread pain and these potential social mediators. Exemplars of previous research identified are discussed below.

(i) Social support

Social support, in the form of one close confidant or a network of personal relationships, has been associated with a reduced risk of the development of physical health problems (Melchior et al, 2003), including myocardial infarction (Dickens et al, 2004) and cardiovascular disease (Everson-Rose & Lewis, 2005). Social isolation has been associated with increased all-cause and breast cancer related mortality (Berkman & Syme, 1979; Kroenke et al, 2006). The absence of social support has been associated with CWP cross-sectionally (Bergman, 2005), whilst the presence of adequate social support was found to be protective of CWP development over a three year prospective study (Bergman et al, 2002). The presence of social support may decrease the stress response by suppressing cortisol during stress exposure (Ditzen et al, 2008; Heinrichs et al, 2003). Improved immune functioning (Zuckerman & Antoni, 1995) and improved recovery from surgery (Vaz-Leal et al, 2011) have also been associated with the presence of social support.

(ii) Adult attachment style

Attachment theory, originally proposed by Bowlby, suggests that individuals form beliefs about themselves and others based on early experiences with caregivers (Bowlby, 1969). This leads to the development of an attachment style which then determines how the individual interacts with others and how they interpret the actions of others (Bowlby, 1969). Four basic styles of attachment have been identified (Bartholomew & Horowitz, 1991). Individuals with a secure attachment feel themselves to be worthy of care and trust that others will be accepting and responsive. Secure attachments are the result of consistent responsive early care giving (Ciechanowski et al, 2001). A dismissing attachment style is characterised by a

negative view of others but a positive view of the self. This style often results from consistent emotional unresponsiveness of the caregiver and leads an individual to become self-sufficient. Conversely, inconsistent emotional responsiveness can lead to a preoccupied attachment style, in which individuals view themselves negatively (i.e. as not being worthy of care). Individuals with this style view others positively and often strive for acceptance from others. Finally, individuals with the fearful style have a negative view of themselves and others as a result of constant criticism or rejection of the caregiver. Although a psychological construct, attachment style determines beliefs concerning social situations, and thus how individuals respond to stressful situations (Bowlby, 2007).

In Meredith et al's (2008) attachment diathesis model of chronic pain, attachment is proposed as a either a mediator or moderator of the relationship between stress and pain. This model proposes that in response to stress, cognitive, behavioural and emotional reactions are influenced by attachment style. So individuals with insecure attachment styles appraise the stressful event more negatively, feel less able to cope and use maladaptive coping strategies, such as catastrophising. This not only results in chronic pain outcomes, but also negatively affects adjustment to pain. In support of this, a community based study including 2,509 participants, found that participants meeting the ACR criteria for CWP were more likely to report an insecure attachment style compared to pain free participants: preoccupied (RRR 2.6; 95% C.I. 1.8–3.7), dismissing (RRR 1.9; 95% C.I. 1.2–3.1), fearful attachment style (RRR 1.4; 95% C.I. 1.1–1.8) (Davies et al, 2009). Compared to individuals with a secure attachment, those with a dismissing attachment style were almost three times more likely to report a higher number of pain sites (RRR 2.8; 95% C.I. 1.2–2.3) (Davies et al, 2009). A fearful attachment style has also been associated with a slower recovery from the physical arousal of stress (Halpern et al, 2011) whilst a secure attachment style has been shown to reduce anxiety to stressful experiences (Ditzen et al, 2008).

In summary, social support and adult attachment style have been associated with both psychological stress and widespread pain. The trauma diathesis stress model of widespread pain therefore proposes that the availability of social support and a secure attachment style, by offering protection from the effects of psychological stress, would reduce the risk of the development of widespread pain. Conversely, an insecure attachment style and lower levels of social support could exacerbate the effects of psychological stress, increasing that risk.

This section examined biological, psychological and social mediators of the stress pain relationship proposed by the trauma diathesis stress model of widespread pain. Empirical evidence has been presented, along with related psychological theory, to demonstrate how these factors are affected by psychological stress and could potentially act as mechanisms by which psychological stress may lead to the development of widespread pain. The following section examines the proposed moderators of the stress pain relationship.

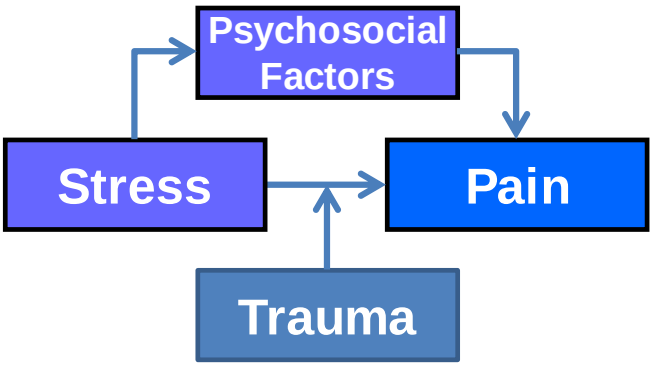
2.5.3 Moderators of the stress pain relationship

The trauma diathesis stress model of widespread pain proposes two potential causes of such susceptibility (moderators): trauma and sex.

a) Trauma

This section examines how traumatic experiences in childhood and adulthood could potentially increase an individual's susceptibility to widespread pain when stressed and the impact of trauma on the proposed psychosocial mediators of the stress pain relationship (Figure 2.7).

Figure 2.7 Trauma diathesis stress model: Trauma, stress, widespread pain and psychosocial mediators



(i) Trauma and the stress pain relationship

As stated above, the long term psychological consequences of trauma have long been understood. Specifically, the experience of childhood abuse and neglect has been associated with psychosis (Fisher et al, 2010), panic disorders, hallucinations (Anda et al, 2006), self-esteem problems, substance abuse, phobias, obsessions, social impairment and relationship problems (Dube et al, 2005), personality disorders (Maniglio, 2009), anger (Springer et al, 2007), post-traumatic stress disorder (Chen et al, 2010) and cognitive deficits (Hedges & Woon, 2011). Of particular interest to the current investigation, childhood abuse has also been associated with an increased risk of anxiety, depression (Springer et al, 2007), somatisation (Anda et al, 2006) and sleep problems (Abrams et al, 2008). It is clear that the experience of childhood abuse significantly increases the risk of a wide range of psychological disorders and also conveys a substantial probability of psychological stress in later life.

Traumatic experiences, particularly during sensitive periods of development, can result in physiological disruptions to the nervous, endocrine and immune systems and allostatic load (Popa et al, 2008; Pesonen et al, 2010). These changes are believed to alter the thresholds and sensitivity of the stress and pain processing system (Heim et al, 2010), as described in Section 2.4.1, Figure 2.1 (pg46). Such disruptions, particularly in the hypothalamic–pituitary–adrenal axis, have been associated with both childhood interpersonal trauma (Heim et al, 2002; McLean et al, 2005a) and adult

physical trauma (Yehuda, 2002; McLean et al, 2005b). For example, childhood physical abuse has been associated with flattened diurnal cortisol rhythm and childhood sexual abuse with increased wakening cortisol levels (Weissbecker et al, 2006). The trauma diathesis stress model of widespread pain therefore proposes that traumatic experiences result in psychological and physiological alterations which increase an individual's susceptibility to widespread pain when they become stressed.

As with childhood interpersonal trauma, problems such as anger, guilt, shame (Amstadter & Vernon, 2008), fear and fatigue (Andersson et al, 1997) are common following adult physical trauma. Adult physical trauma has also been associated with psychological stress, including anxiety, depression and sleep problems (Andersson et al, 1997; Gargan et al, 1997; Mayou et al, 2001; Smith et al, 2008).

(ii) Trauma and the stress pain mediators

The proposed psychosocial mediators of the stress pain relationship have all been empirically associated with traumatic experiences: dissociation (Merckelbach & Jelicic, 2004; Irwin, 1996; Brown, Schrag & Trimble, 2005; Walker et al, 1992; Badura et al 1997; Mulder et al, 1998; Salmon et al, 2003; Roelofs et al, 2002; Nijenhuis et al, 1998), health anxiety (Fiddler et al, 2004; Stein et al, 2004), somatosensory amplification (Walker et al, 1992; Gurevich et al, 2004), personal control (Mills et al, 2007), attachment style (Waldinger et al, 2006; Aspelmeier et al, 2007; Bowlby et al, 2007) and social support (Brewin et al, 2000; Runtz & Schallow, 1997; Alvarez & Hunt, 2005). In terms of the trauma diathesis stress model of widespread pain, it is proposed that the mediation of the stress pain relationship by these psychological and social factors will be different in individuals who have experienced a trauma compared to those who have not.

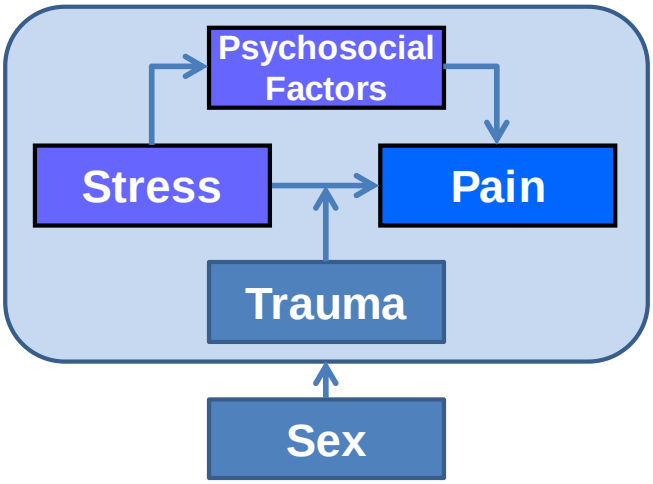
In summary, trauma experiences have long been associated with psychological and physical ill health. However, the findings from research exploring a direct association

between widespread pain and both childhood interpersonal and adult physical trauma are inconclusive. These research findings suggest that traumatic experiences are not sufficient on their own for the development of widespread pain, but that traumatic experiences may increase sensitivity to psychological stress, changing the relationship between psychological stress and widespread pain. This lead to the development of the proposed trauma diathesis stress model of widespread pain, whereby traumatic experiences create a susceptibility (diathesis), which is only activated by psychological stress.

b) Sex

In addition to trauma, sex is also proposed as a moderator of the stress pain relationship. The prevalence of pain and psychological stress is typically higher in females than males (Branco et al, 2010) and sex differences have also been found in the response to pain, psychological stress and trauma, as described below. Based on this evidence, the trauma diathesis stress model proposes that the relationship between psychological stress and widespread pain and the effect of trauma will be different in males and females, as shown in Figure 2.8.

Figure 2.8 Trauma diathesis stress model – Trauma, sex, stress, widespread pain and psychosocial mediators



Sex differences in the prevalence of widespread pain and FM have been found by a large number of studies. Estimates of the female male ratio vary between two to one

(Branco et al, 2010) and six to one (Kurtze & Svebak, 2005), although there are some exceptions (e.g. Gupta et al, 2007). A female predominance also exists with regard to anxiety, depression (Kurtze & Svebak, 2005) and somatisation (Barsky et al, 2001; 2005). With regard to any differences between males and females in the impact of widespread pain, research findings are mixed. Gjesdal et al (2011) found that females have a 44% higher risk of receiving a disability pension than men as a result of their FM, when adjusting for age, education, income, weekly working hours and caring for children. However, Buskila et al (2000), found males to have more severe symptoms, decreased physical function, and lower quality of life than females.

The hormonal contribution to pain is suggested by the increase in chronic pain conditions in females following puberty and the menopause (see Figure 1.1 pg8 and Figure 1.3 pg12). The severity and frequency of symptoms also vary during the menstrual cycle and decrease during pregnancy (Fillingim et al, 2009). Aloisi et al (2007) studied the effects on pain in transsexuals undergoing hormone replacement therapy; oestrogen and progesterone for male-to-female and testosterone for female-to-males. Of the male-to-female participants 23% developed chronic headaches, breast or musculoskeletal pain, whilst pain conditions improved in 55% of the female-to-male participants. However, the evidence is not conclusive; other studies have found no significant differences in pain perception across the menstrual cycle or related to the use of exogenously administered hormones (Racine et al, 2012).

In a recent review, Fillingim et al (2009) found sex differences in experimentally induced pressure, heat, cold and electrical pain stimulation, with females demonstrating lower pain thresholds and tolerance than males. Similar findings were also evidenced in temporal summation and tonic pain, although no differences were found in ischaemic pain stimulation. Brain imaging studies, using positron emission tomography and functional magnetic resonance imaging, have also found sex differences in the patterns of activation in experimental pain tasks, however, the differences in methodology make

drawing firm conclusions difficult (Fillingim et al, 2009). Again, the evidence is not conclusive; a recent review by Racine et al (2012) found no significant difference in pain perception between males and females.

Sex differences have also been found in reactivity to stress. In a systematic review, Ordaz and Luna (2012), found that compared to males, females react to stressful situations with more subjective negative affect, but lower physiological arousal. Interestingly, these differences emerged during adolescence, further implicating the role of hormones in sex differences. Research also suggests that males and females experience different types of trauma (Radford et al, 2011) and react differently to traumatic experiences (Christiansen & Elklit, 2008). For example, in the recent NSPCC study, the prevalence of childhood physical abuse and neglect was similar for males and females, but the rates for childhood emotional and sexual abuse were significantly higher for females in this study (Table 2.3). Maschi et al (2008) found sex differences in the methods employed to cope with traumatic experiences. Whilst male childhood abuse victims employed an externalising, aggressive coping style, female victims adopted internal coping strategies, directing aggression inwardly. The results of this difference manifest as delinquent behaviour in males, and increased levels of depression and anxiety in females. This may account for the increased prevalence of widespread pain in females.

Table 2.3 Prevalence of childhood abuse and neglect by gender and type

	Childhood abuse type			
	Physical	**Emotional**	**Sexual**	**Neglect**
Male	10.9%	4.7%	1.6%	10.7%
Female	9.0%	7.4%	8.5%	9.1%

Radford et al, 2011, pg157

Clearly the evidence outlined above on the difference between males and females suggests that sex is an important factor for both psychological stress and widespread pain. Sex differences are evident in the prevalence and impact of widespread pain (and

FM), and are suggested in pain perception and reactions to psychological stress and trauma. In terms of the trauma diathesis stress model of widespread pain, it is hypothesised that sex will moderate the relationship between trauma, psychological stress and widespread pain.

2.5.4 Summary of the trauma diathesis stress model of widespread pain

The trauma diathesis stress model of widespread pain proposes a direct association between psychological stress and widespread pain, mediated by psychosocial factors and moderated by trauma and sex. Empirical evidence has been presented to show that anxiety, depression, somatisation, sleep problems and life events individually and combined have consistently been associated with the development and persistence of widespread pain. Research evidence also shows that psychological stress affects psychological and social processes. These alterations possibly lead to dissociations between sensation and perception, heightened concern regarding one's health and a reduced perception of personal control, resulting in a misinterpretation of amplified bodily processes. Psychological stress may also lead to widespread pain via inadequate social support and an insecure attachment style.

As outlined, traumatic experiences can result in changes to the stress, pain and immune systems. The resulting increased reactivity to subsequent stressors may leave the individual susceptible to widespread pain. Traumatic experiences may also lead to psychological and social problems. An individual who has experienced dissociation as the result of a trauma is likely to use the same unconscious defence mechanism when faced with psychological stress. Concerns for health and a bodily focus may be increased, whilst social support, security of attachment and feelings of control may be reduced by the experience of trauma. Males and females experience different types of trauma and differ in their reactions to trauma. The susceptibility towards widespread pain when stressed may therefore be different in males and females and dependent upon whether they have experienced a trauma or not.

The trauma diathesis stress model of widespread pain aims to identify who is at risk of developing widespread pain when faced with psychological stress and to clarify how psychological stress leads to widespread pain. The identification of susceptible individuals and the mechanisms by which they develop widespread pain have implications for the treatment of widespread pain.

2.6 Current treatments for widespread pain

Current treatments for widespread pain include pharmacological and non-pharmacological interventions such as physical and psychological therapies. These treatments are summarised below with reference to their effectiveness in targeting the proposed mediators of the stress pain relationship: dissociation, health anxiety, somatosensory amplification, personal control, adult attachment style and social support.

Pharmacological treatments for widespread pain include agents which act at the peripheral level, such as non-steroidal anti-inflammatory drugs and those having effects on the central nervous system, such as the analgesic tramadol (Yunus & Aslan, 2004) and anti-anxiety and anti-depressant medications. These include serotonin-norepinephrine reuptake inhibitors (Marks et al, 2009), tricyclic agents and selective serotonin reuptake inhibitors (Yunus & Aslan, 2004). Anti-depressant medications have been found to result in mild improvement in fatigue and moderate improvements in sleep, well-being and pain (O'Malley et al, 2000). However, adverse effects from these medications can affect up to a third of patients (Marcus, 2009) and as a result, patients often discontinue their use. Furthermore, the benefits do not persist once treatment has ended (van Koulil et al, 2007).

Non-pharmacological physical treatments include education, exercise, relaxation and biofeedback. Education strategies include providing descriptions of pain physiology and central sensitisation (Nijs et al, 2011) which reassure the patient that the condition is not life threatening or associated with tissue damage. Advice on general health behaviours,

such as good eating and sleeping habits, regular exercise, weight loss and smoking cessation can also be provided (Yunus & Arslan, 2004). When combined with medication and exercise, education has been shown to be effective at reducing experimental pain intensity ratings and improving physical functioning, general and mental health, personal control and self-efficacy in FM patients (van Oosterwijck et al, 2013). Exercise, including aerobic and strength training, targets deconditioning (Busch et al, 2011) and reduces stress (Bote et al, 2013). Relaxation and biofeedback are also effective for stress reduction, decreasing both sleep problems and depression (Glombiewski et al, 2010).

Psychological therapies include cognitive behavioural therapy (CBT), mindfulness and behavioural therapies, and eye movement desensitisation and reprocessing (EMDR) (Glombiewski et al, 2010). CBT is an umbrella term for a variety of components that can be tailored to meet individual needs, although it often takes place in a group setting (van Koulil et al, 2010). In a recent meta-analysis, Glombiewski et al (2010) found that CBT resulted in small to moderate improvements in depression, functional status, sleep problems and pain intensity for FM patients. Mild improvements have also been found in both health anxiety (d=0.4) and somatosensory amplification (d=0.4) with the use of attention focused CBT (Weck et al, 2013; Hedman et al, 2013).

The aim of CBT in pain treatment is usually the management of symptoms, with little focus on encouraging the expression and processing of avoided emotional information, which may be of benefit to individuals who have experienced a trauma (Lumley, 2011). EMDR was developed in the late 1980s by F. Shapiro (2012) as a therapy specifically for the treatment of “traumatic stress and distressing life experiences” (E. Shapiro 2012 pg242). As with CBT, variations of the EMDR protocol have been developed and applied to treat dissociation and attachment disorders (Regehr et al, 2013; Wesselmann et al, 2012), fatigue, phantom limb pain and chronic pain conditions (van Rood & de Roos, 2009). Two studies have examined the effectiveness of EMDR in FM patients. Friedberg (2004) provided two EMDR treatment sessions to six female FM patients, whilst Teneycke

(2012) used 12 sessions with three female FM patients. Both trials resulted in decreases in anxiety, depression and pain and improvements in sleep and communications with others, improvements which were maintained for at least three months post-treatment. However, both Friedberg et al (2004) and Teneycke's (2012) studies involved only a small number of female participants with no control group comparisons, hence making generalisations difficult.

Individual psychodynamic psychotherapy has also been successful in the treatment of chronic pain conditions, but only in individuals with a history of trauma. For example, Creed et al (2005) found that eight sessions of individual psychodynamic psychotherapy over three months lead to greater improvements in irritable bowel pain and physical function in individuals reporting childhood sexual abuse than those without such a history. This therapy allowed an exploration of symptoms, emotions, and links between symptoms and emotions and the benefits seen following treatment improved further in the 12 months following treatment. Similarly, Guthrie et al (2004) found that irritable bowel patients with a history of sexual abuse showed increased tolerance to rectal distension following psychotherapy, whereas a decrease in tolerance was found in those without reported abuse.

Treatments for widespread pain already contain components that target stress and the proposed mediators of the stress pain relationship. Overall, pharmacological and non-pharmacological treatments for widespread pain achieve only small to moderate symptom improvements. Not all patients benefit from the same interventions (Turk, 2005; O'Malley et al, 2000; Richards & Scott, 2002). Tailoring treatments to subgroups of patients would not only be beneficial for the patient, but would also be cost effective, as treatments would be prescribed only for individuals who are most likely to benefit (Hill et al, 2011). By identifying individuals at the greatest risk of developing widespread pain and providing a greater understanding of the mechanisms involved in the development of widespread pain, the results of this study will inform effective risk reduction and treatment strategies.

2.7 Rationale for thesis

Research evidence outlined in this chapter has shown psychological stress to be consistently associated with the development and persistence of widespread pain, but also that not everyone who experiences psychological stress goes on to develop widespread pain. This suggests that some individuals are more susceptible than others to the development of widespread pain when they experience psychological stress. The trauma diathesis stress model of widespread pain proposes trauma and sex as the cause of such susceptibility. It is proposed that the equivocal findings of the current research (see Tables 2.1 and 2.2) are due to the way in which the relationship between trauma and widespread pain has been examined. These studies have explored a direct link between trauma and widespread pain, without considering the role of psychological stress. These issues will be addressed in the current study as follows.

The trauma diathesis stress model of widespread pain proposes that traumatic experiences are insufficient on their own for the development of widespread pain, but that they create a susceptibility which is later activated by psychological stress. The evidence from research offers greater support for this approach than for a direct association between trauma and widespread pain. Widespread pain may not be a direct response to traumatic experiences, but may be related more to the individual's reaction to the trauma and subsequent stressful experiences. This study therefore examined traumatic experiences as a moderator of the stress pain relationship. With regard to childhood trauma, this study examined not only the effect of the individual types of childhood abuse and neglect, but also the effects of the frequency of abuse and multiple types of abuse. In addition, rather than assessing pain dichotomised according to the ACR criteria, this study examined the "widespreadness" (Natvig et al, 2010 pg71) of pain using a count of the number of pain sites. Widespread pain results from a complex interaction of multiple factors (Clauw & Crofford, 2003) for which sophisticated analytical techniques, as proposed in the current study, would be appropriate (Van Houdenhove et al, 2005). In

order to ascertain a clearer picture of the relationship between trauma, stress and widespread pain, the method used in this thesis is structural equation modelling. This allows for the examination of the moderators (in whom) and mediators (how) of the stress pain relationship, whilst controlling for potential confounding variables (as detailed in chapter 4).

Researchers investigating the relationship between childhood interpersonal trauma and chronic pain conditions suggest that screening for such trauma takes place within primary care settings (Leserman et al 1998; Van Houdenhove et al, 2001; Green & Kimberling, 2004; Friedman et al, 1992; Sachs-Ericsson et al, 2009). At this point, however, the evidence for the relationship does not appear conclusive enough to warrant such a step. However, the findings are intriguing and the recent success of a targeted intervention for individuals with a history of childhood sexual abuse and irritable bowel (Creed et al, 2005) indicate that the relationship between trauma and widespread pain deserves further investigation. Even sceptics of the association recognise the need for more tightly controlled and sophisticated studies (Raphael et al, 2004).

2.8 Chapter summary

This chapter presented reviews of the research evidence exploring direct associations between trauma and widespread pain, and psychological stress and widespread pain. An examination of the current theoretical models of trauma and widespread pain, found that none of the existing models could suitably explain the empirical evidence. A trauma diathesis stress model of widespread pain was therefore developed. Each element of the model was examined in light of current theoretical understanding and evidence from the research literature. The proposed studies seek to address a number of the methodological issues described above by using a population based longitudinal cohort design, and by employing sophisticated statistical techniques to match the complexity of widespread pain's aetiology. This will enable a more thorough understanding of relationship between trauma, stress, widespread pain and psychological, social and

behavioural factors, and provide a clearer understanding of the pathway from trauma to widespread pain. This information can inform treatment trials and has implications for both primary and secondary prevention. For example, the early identification of at risk individuals may help prevent the development of widespread pain, whilst tailored treatments may be used to reduce effects once it has developed.

Chapter 3 Aims and objectives

3.1 General Aim

The aim of the analyses presented in this thesis was to ascertain whether individuals with a history of trauma have an increased susceptibility to widespread pain when they experience psychological stress.

3.2 Hypotheses

This research assesses the trauma diathesis stress model of widespread pain, to test the hypotheses that:-

(1) Among adults, an increase in psychological stress is associated with an increase in the number of pain sites.

(2) The relationship between psychological stress and number of pain sites will be moderated by exposure to traumatic experiences and by sex.

(3) The relationship between psychological stress and number of pain sites will be mediated by adult attachment style, social support, health anxiety, somatosensory amplification, dissociation and personal control.

(4) The mediation of the stress pain relationship by adult attachment style, social support, health anxiety, somatosensory amplification, dissociation and personal control will be moderated by traumatic experiences and sex.

Chapter 4 Statistical analysis

4.1 Chapter overview

Data from two population based prospective studies was used to identify whether individuals with a history of trauma have an increased susceptibility to widespread pain when they experience psychological stress. Details of the statistical analysis common to both studies are presented in this chapter. The study design, procedures, sampling frame and measures for the General Practice Symptom Survey (GPSS) and the North Staffordshire Osteoarthritis Project (NorStOP) are described in chapters 5 and 8 respectively. All analysis was carried out using IBM SPSS (Statistics Package for Social Sciences) version 20.0 and AMOS (Analysis of Moment Structures) version 21.0.

4.2 Data distribution

The distribution of both the GPSS and NorStOP data was assessed using the Kolmogorov-Smirnov statistic with Lilliefors' significance. The null hypothesis for this test is that the data are normally distributed; test results that are significant therefore indicate that the data is not normally distributed. For the comparison tests between participants and non-participants and the descriptive analysis, non-parametric analysis was used for non-normally distributed data. Correlation analysis used Pearson's product moment correlation. This test has been shown to be extremely robust to violations of distribution, so can be used for both normally and non-normally distributed data (Chok, 2008; Norman, 2010). Furthermore, the issues arising from non-normal distributions within data can be overcome in structural equation modelling (SEM) with the use of bootstrapping. Parameter estimates (e.g. regression weights, means etc.) were calculated for multiple samples, enabling confidence intervals to be constructed (Byrne, 2010).

4.3 Comparison of participants and non-participants

In order to assess potential response bias, comparisons were made between participants and non-participants at baseline and follow up using the Chi squared test for

categorical data (for example sex) and the Mann Whitney U test for continuous data (for example age). Data allowed comparisons on age, sex and general practice (and version of the questionnaire for GPSS, see section 5.2, pg95 for details) between participants and non-participants at baseline. All data collected from responders at baseline was available to compare participants and non-participants at follow up. The results of these comparisons are presented in Chapter 6 for the GPSS data and Chapter 9 for the NorStOP data.

4.4 Descriptive analysis

Frequencies with percentages or medians with interquartile ranges where appropriate, were calculated for all variables. A description of the "widespreadness" (Natvig et al, 2010, pg71) of pain using a count of the number of pain sites and the prevalence of traumatic experiences within the study population are presented. Mann Whitney, Kruskal Wallis and Pearson correlations analysis where appropriate were carried out to describe the associations between the number of pain sites and demographic, predictor, mediator and moderator variables for each study. The results are presented in Chapter 7 for the GPSS data and Chapter 10 for the NorStOP data.

4.5 Missing data

There are a number of reasons why responses may be missing from a dataset. Participants may fail to answer a question due to a misunderstanding of the question, a perceived inability to answer the question, or because the question is of a sensitive nature. There are consequences of missing data. Missing data can reduce statistical power and can undermine the representativeness of the sample leading to potential bias within the observed associations. Missing data should be examined to understand the potential for bias and suitably addressed, where possible (Kang, 2013).

Three categories of missing data have been identified; missing completely at random (MCAR), missing at random (MAR) and not missing at random (NMAR). If there are no

patterns to the missing data, indicating no relationship between the missing variable(s) and other variable(s) then the data is said to be MCAR. Data is classed as MAR where there are patterns to the missing data, such that the missing data can be explained by data that is available, but is independent of missing variables. Data is classed as being NMAR if the missingness is dependent upon what the value would have been, for example, if income data was missing from only those participants with the highest or lowest incomes (Enders, 2011; Schlomer et al, 2010). Distinguishing these patterns informs the techniques available to deal with the missing data. When data is MCAR and the rate of missing data is less than 5%, then imputation using maximum likelihood estimating techniques provides accurate replacement values (Enders, 2011; Schafer & Graham, 2002; Schafer, 1999).

Little's Missing Completely at Random test was used to identify whether the data was missing completely at random (Little, 1988). The null hypothesis for this test is that the missing data are MCAR. Thus a non-significant result indicates that the data are MCAR and suitable for imputation, whilst a significant result indicates that the data are either MAR or NMAR. No test is currently available to distinguish between these (IBM, 2009). Data found to be MCAR was imputed using the estimation maximisation function within SPSS. Little's MCAR test does not require data to be normally distributed (Little, 1988).

As recommended by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (von Elm et al, 2007), the amount of missing data and an explanation of how missing data was addressed, in each of the datasets, is presented in Sections 7.4 for the GPSS study and 10.3 for the NorStOP study.

4.6 Structural equation modelling (SEM)

As described in Section 1.2 (pg1), research suggests that widespread pain results from a complex interaction of multiple factors (Meredith et al, 2008). SEM has been used to examine the complex interactional relationships between childhood trauma, stressful life

events and depression in chronic lower back pain and chronic pelvic pain (Lampe et al, 2003), and between childhood and adult interpersonal abuse, post-traumatic stress disorder and chronic pain (Wuest et al, 2009). SEM allows for the simultaneous assessment of multiple factors, moderation and mediation analysis (Byrne, 2010), and is therefore ideally suited for the investigation of the widespreadness of pain.

There are three main approaches to SEM (Schumacker & Lomax, 2004):-

a) Confirmatory approach. A single theoretical model is developed and tested to ascertain how well the model fits the collected data. This approach was used for the assessment of the association between stress and pain, the moderation effects of trauma and sex and mediation analysis. Further details are outlined below.

b) Alternative models. In this approach a limited number of models are created based on different theoretical explanations of the data. The models are then compared to assess which best explains the data. This approach was used to identify the most appropriate model for prospective analysis (see Section 4.6.6, pg90).

c) Model generating. An initial model is created and assessed as to how it fits the data. Modification indices are then inspected and used to amend the model until the best fit is found for the data, whilst maintaining theoretical and practical meaning. This approach was not used in the current studies.

SEM uses a combination of confirmatory factor analysis, multiple linear regressions and multiple group comparison analysis. Whilst each of these techniques could be performed individually within many software packages including SPSS, the use of SEM has a number of benefits:

- All analysis is performed simultaneously.
- An assessment is included of measurement error (as described below).

- Multiple group analysis enables a comparison of the critical ratios (as described in Section 4.6.3).
- Latent variables are created from multiple observed variables (as described in Section 4.6.1) and therefore represent a more reliable measure (Hopwood, 2007) which is more reflective of the underlying construct than a single measure (Lei & Wu, 2007). The relationship between the created latent variables and between the latent variables and observed variables can be assessed within one model.
- The graphical interface within packages such as AMOS allows models to be quickly specified using simple drawing tools (see examples in figures 4.1 – 4.6). The results of the analysis are then presented pictorially, aiding interpretation (for example, see figures in chapters 7 and 10) (Arbuckle, 2012).

AMOS provides estimates for each parameter within the model. The strength of the relationships between variables is indicated by regression weights (standardised β and unstandardized B) and the amount of variance in outcome variables explained by the model is provided by multiple squared correlations (R^2). Based on the recommendations from research, a maximum likelihood procedure, based on bootstrap of 3,000 was used to produce 95% bias corrected confidence intervals (Sharma & Kim, 2012; Byrne, 2010; Preacher et al, 2007; Efron & Tibshirani, 1985).

> *"The goal of SEM analysis is to determine the extent to which the theoretical model is supported by sample data"*
>
> (Schumacker & Lomax, 2004, pg 2).

Model fit indices are different ways of expressing the difference between the model and the observed data (Blunch et al, 2013). Over 20 different model fit statistics are available within AMOS (Arbuckle, 2012), with different indices representing different aspects of model fit (Hu & Bentler, 1998). The most commonly used measure of fit is the Chi squared goodness of fit index (Singh, 2009); however, as this test becomes unreliable with sample sizes in excess of 400 (Kenny, 2014), it was not used to assess the models in

these studies. Research by Hu and Bentler (1998; 1999) suggests the use of a two index presentation strategy combining Standardised Root Mean Square Residual (SRMR) and Root Mean Square Error of Approximation (RMSEA) tests. The Root Mean Square Residual (RMR) test is the square root of the difference between the residuals of the sample and model; however, this is difficult to interpret (Byrne, 2010). The Standardised RMR (SRMR) ranges from zero to 1.0, with zero indicating a perfect fit (Byrne, 2010). The RMSEA "gives the average amount of misfit for a model, per degree of freedom" (Bagozzi & Yi, 2012, pg28). Both the RMSEA and SRMR tests have been shown to be less sensitive to distribution and sample size, but more sensitive to model misspecification (Hu & Bentler, 1998). Following Hu and Bentler's (1998, 1999) recommendations for use with maximum likelihood estimation, the SRMR (≤0.09) and RMSEA (≤0.06) tests were used to assess model fit in these studies.

The Akaike Information Criterion (AIC) test examines both the statistical goodness of fit and the number of parameters (Byrne, 2010). The AIC is used to compare models that are estimated using the same data; the model with the smallest AIC value being the most parsimonious (Hooper et al, 2008). This test was used to compare two prospective models (see Section 4.6.6).

Aspects of the trauma diathesis stress model of widespread pain were assessed by progressively more complex models. The remainder of this chapter describes the theory behind each of these models, provides an example of how the model was used within this analysis and describes how the results of the analysis are presented.

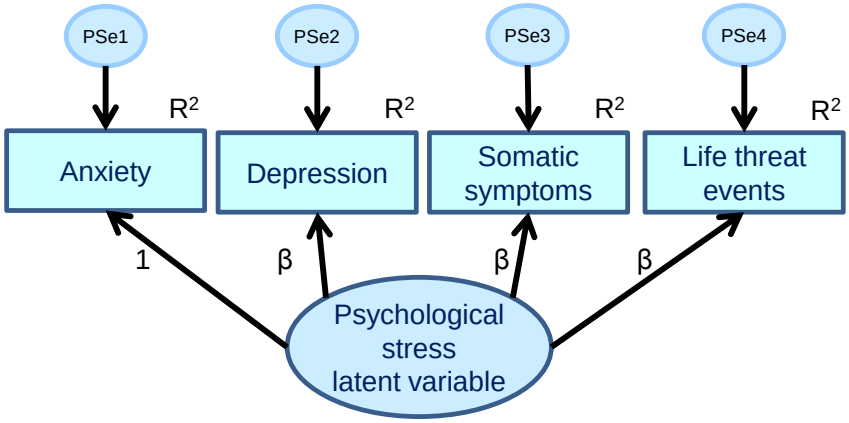
4.6.1 Latent variables

SEM uses two types of variables; observed variables and latent variables. Observed or manifest variables are those items that are directly measured. Scores collected on a questionnaire, such as the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983), are examples of manifest or observed variables. Latent variables represent

underlying theoretical constructs which are “operationalised” using a number of observed variables hypothesized to reflect those underlying constructs (Blunch, 2008, pg7). For example, scores on tests of verbal and numeric ability would be influenced by an individual’s underlying intelligence.

Figure 4.1 shows an example of a latent variable. In the GPSS study, data was collected for anxiety, depression, somatisation and life threatening events. In SEM notation, such observed variables are depicted by squares or rectangular boxes.

Figure 4.1 Example latent variable



Square or rectangle = observed variable; circle or ellipse = unobserved latent variable; PSe1-4 = error terms for anxiety, depression, somatic symptoms and life threatening events; R^2 = variance of observed variable explained; β = standardised regression coefficient

It is hypothesised that these items would reflect an individual’s level of underlying psychological stress. In SEM, such unobserved variables are represented by circles or ellipses. Single headed arrows represent the impact of one variable on another. In drawing a latent variable, the arrows go from the latent variable to the observed measures. The underlying construct of psychological stress is created by assessing the common variance amongst the observed variables using confirmatory factor analysis. Estimates of participants’ scores on the latent variable can be created within AMOS using regression imputation. These scores can then be used in subsequent statistical analysis (Campbell et al, 2007; Sieri et al, 2004; Joreskog, 2000; Joreskog et al, 2006).

Each observed variable within Figure 4.1 also has an error element (Psychological stress error [PSe1 to PSe4]). The variable error, depicted by a circle because it is not directly observed, represents measurement error and the variance in the observed variable that is not explained by the latent variable (Blunch, 2013). In order to solve the set of simultaneous equations for the latent variable, there must be sufficient known information. A model is said to be "identified" if the number of known parameters is equal to or exceeds the number requiring estimation (Kenny, 2014). When creating a latent variable it is necessary to fix at least one path coefficient to 1.0 (as from the psychological stress latent variable to anxiety in Figure 4.1). This aids the identification process by reducing the number of parameters that are required to be estimated and also sets the scale for the latent variable (Byrne, 2010).

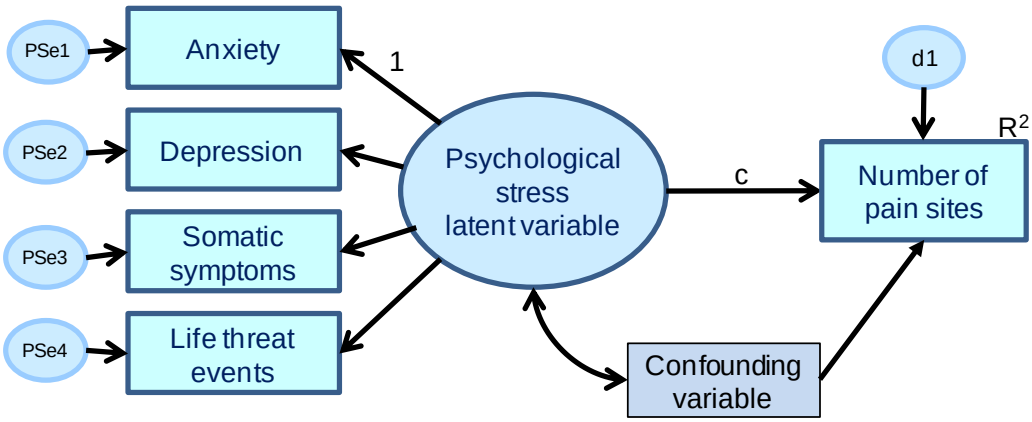
Results for the latent variables created in this study are presented in models and tables. In the models, the standardised regression coefficients (β) are shown on the connecting arrows. These indicate the strength of the associations; for example the number of standard deviations by which anxiety changes as the result of one standard deviation increase in the psychological stress latent variable. The variance explained for each observed variable (R^2) will be displayed above (or to the right of) the outcome box. The 95% confidence intervals for the standardised and unstandardised regression coefficients (B) are presented in the accompanying table.

Within the Trauma diathesis stress model of widespread pain, two latent variables are proposed. Psychological stress was measured using the observed variables of anxiety, depression, somatisation and life threatening events in the GPSS study (see Section 5.5) and anxiety, depression and sleep problems in the NorStOP study (see Section 8.5). In the GPSS study, childhood abuse and neglect was measured using the observed variables of childhood physical, emotional and sexual abuse, combined with the maternal care scale of the Parental Bonding Instrument (see Section 5.5).

4.6.2 Basic predictor outcome models

The structural or path model pictorially represents the relationship between variables, which can be latent or observed. Predictor variables have no single headed arrows pointing towards them. They are the beginning of the path model. Outcome variables have at least one single headed arrow pointing towards them. Figure 4.2 shows an example of a structural model containing one latent variable, psychological stress; one observed outcome variable, number of pain sites; and a confounding variable. The relationship between the psychological stress latent variable and the number of pain sites is indicated by path c. In a similar way to the errors associated with the observed variable in a latent variable model, outcome variables have an associated disturbance (d1). This represents the error in the prediction of the outcome variable by the model. The relationships between the variables are assessed simultaneously using multiple linear regression.

Figure 4.2 Example predictor outcome model



PSe1-4 = error terms for anxiety, depression, somatic symptoms and life threatening events; c = standardised regression coefficient between psychological stress and number of pain sites; d1 = disturbance term for number of pain sites; R^2 = variance explained in number of pain sites

A confounding variable is a factor that influences the relationship between the predictor and outcome, but is not theoretically causal. Confounding variables are represented in the model with a single head arrow indicating a direct association with the outcome (number of pain sites) and a bidirectional arrow indicating the covariance or correlation with the predictor (psychological stress). In order to account for the influence of confounding variables within the current study, those demographic factors which were

significantly associated with the number of pain sites in the bivariate analysis were added to the basic predictor outcome model as shown in Figure 4.2. Only those variables maintaining a significant relationship ($p<0.05$) within the SEM were retained.

Results are presented in models and tables. In the models, the standardised regression coefficients (β) are shown on the connecting arrows and the variance explained in the number of pain sites (R^2) is displayed above the outcome box. The 95% confidence intervals for the standardised and unstandardised regression coefficients (b) for path c are presented in the accompanying table.

4.6.3 Moderation models

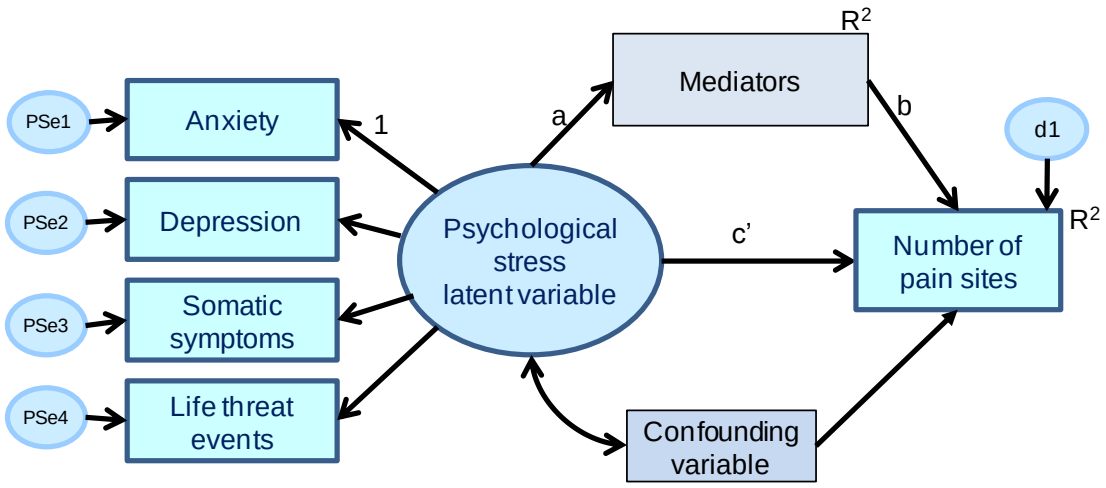
Moderation analysis examines whether the strength or direction of a relationship between a predictor and outcome is dependent upon a moderator variable (Preacher et al, 2007). The trauma diathesis model of widespread pain proposes that the experience of trauma would moderate the relationship between stress and pain. In these analyses, the test for the moderation effect of trauma was assessed using the multiple group analysis (MGA) and pairwise comparison functions within AMOS. MGA allows for the simultaneous analysis of multiple groups of participants, allowing for a comparison of the strength of the stress pain relationship between participants who have and have not experienced a trauma and between males and females. A pairwise comparison is a critical ratio which represents the difference between the coefficients of two pathways, divided by the standard error of the difference (Arbuckle, 2012). The results are interpreted using a table of normal standard distributions. Moderation was said to occur when the regression coefficients for the stress pain relationship differ significantly at $p<0.05$ and $p<0.02$ level (pairwise critical ratio ±1.96 or 2.33, respectively) (Denis, 2010).

Results, including regression coefficients, 95% confidence intervals, R^2 and pairwise comparisons will be presented in Section 7.5 for the moderation effect of childhood abuse and Section 10.3 for the moderation effect of physical trauma in adulthood.

4.6.4 Mediation models

Mediation analysis enables an investigation of the processes by which a predictor affects an outcome. As shown in Figure 4.3, as well as the direct association between the predictor and outcome (path c'), the predictor variable has an effect on the mediator (path a) and the mediator variable in turn has a relationship with the outcome (path b). In Figure 4.2, c indicates the total effect of the predictor variable on the outcome variable, whilst controlling for confounding variables. In Figure 4.3, c' indicates the direct effects of the predictor variable on the outcome variable, when the mediator (and confounding) variables are controlled for. The difference between c and c' is the amount of mediation or the indirect effect. Mediation was said to have occurred when the indirect effects were significant (Rucker et al, 2011).

Figure 4.3 Example mediation model



Total effect = Direct effect + Indirect effect or *c = c' + ab*

PSe1-4 = error terms for anxiety, depression, somatic symptoms and life threatening events; a = standardised regression coefficient between psychological stress and mediator variable; b = standardised regression coefficient between mediator variable and number of pain sites; c' = standardised regression coefficient for the direct path between psychological stress and number of pain sites controlling for mediator and confounding variables; d1 = disturbance term for number of pain sites; R^2 = variance explained in number of pain sites

Details of the mediator variables examined in the current study are provided in Chapters 5 (GPSS) and 8 (NorStOP) and the results are presented in Chapters 7 and 10 respectively.

4.6.5 Moderated Mediation models

Moderated mediation analysis examines whether the explanatory power of the mediator is conditional upon the value of the moderator. The mediation effects in the initial models described in Section 4.6.4 may have been obscured by the moderator. All mediation models were therefore re-examined irrespective of the significance of the indirect effects in the initial model. MGA was used in order to identify whether the effect of the mediator on the stress pain relationship differed based on trauma status and between males and females. In the NorStOP analysis trauma status was dichotomised (yes / no), whilst in the GPSS analysis, three abuse groups were examined (see Section 5.5). Multiple comparisons can increase, by chance, the incidence of Type 1 errors (i.e. the rejection of the null hypothesis when it is true). Bonferroni corrections were used to address this potential issue by dividing the p value by the number of tests. The p value was therefore set to 0.006 in the GPSS moderated mediation analysis. Moderated mediation was said to occur when the indirect effects were significant in one group, but not in another.

4.6.6 The influence of baseline pain in prospective modelling

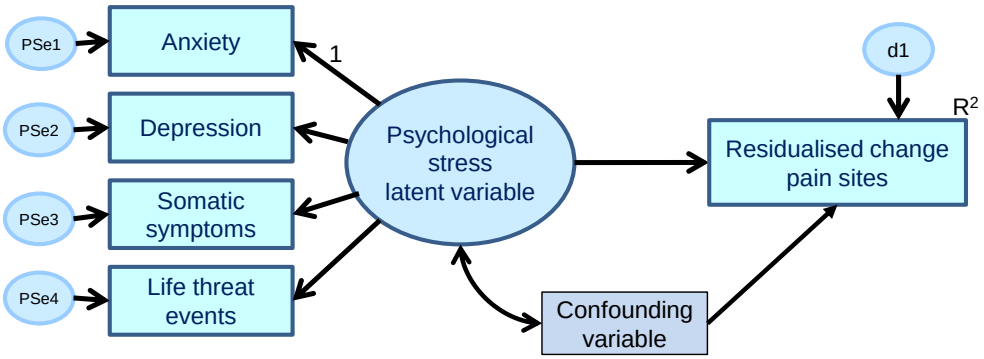
Pain at baseline is a strong predictor of subsequent pain (Gureje et al, 2001). In order to assess the predictive ability of psychological stress on the number of pain sites it is necessary to take into consideration baseline levels of pain. There are a number of methods for accounting for baseline levels of factors in prospective analysis (Raykov, 1993; Glymour et al, 2005). Three alternative approaches (residualised change scores, treating baseline pain as an additional stressor and controlling for baseline pain as a confounder) are described below.

a) Residualised change model

The residualised change score represents the amount of pain at follow up that is not predicted by pain at baseline (Gillespie & Streeter, 1994). Linear regression is used to calculate a prediction of the number of pain sites at follow up based on the number of

pain sites from baseline. Residualised changes scores are the difference between these predicted scores and the actual pain scores observed at follow up. The residualised change model, shown in Figure 4.4, would examine the amount of the change in the number of pain sites that is predicted by baseline levels of psychological stress. As this approach is more appropriate for assessing the effectiveness of interventions (Palmeira et al, 2009; Glymour et al, 2005) it was not used in the current study.

Figure 4.4 Residualised change model

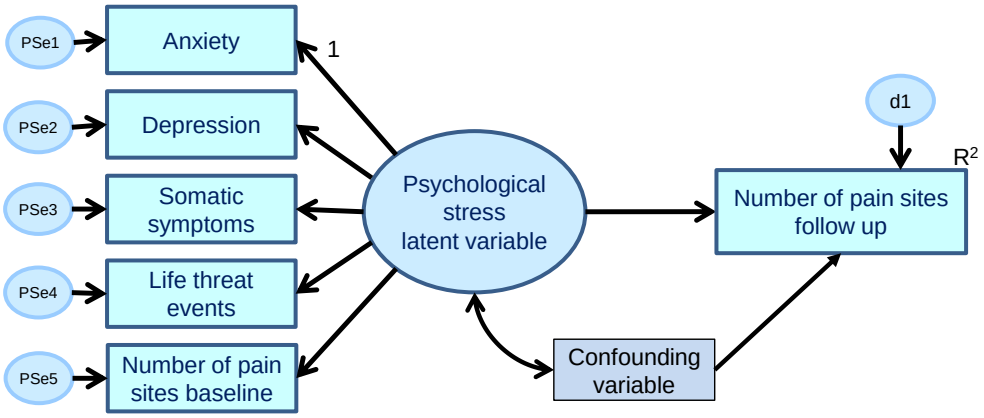


PSe1-4 = error terms for anxiety, depression, somatic symptoms and life threatening events; d1 = disturbance term for residualised change in number of pain sites; R^2 = variance expalined in residualised change in number of pain sites between baseline and follow up

b) Model 1 Pain as a stressor

The diathesis stress models of chronic pain proposed by both Turk (2002) and Meredith et al (2008) hypothesise that pain acts as an additional stressor, increasing the risk of further pain. Figure 4.5 shows an example of a pain as a stressor model. The *psychological stress* latent variable, in this model only, has been constructed from baseline levels of anxiety, depression, somatisation, life threatening events and also baseline levels of pain.

Figure 4.5 Model 1 Pain as a stressor

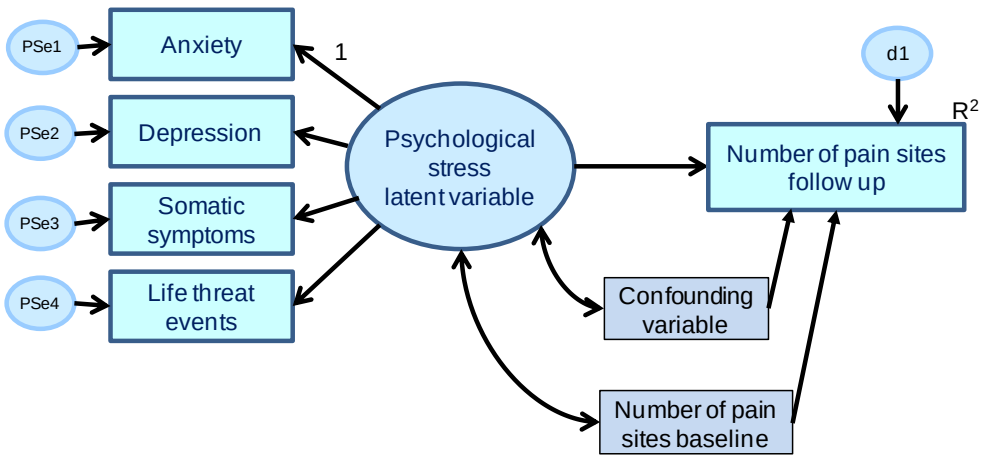


PSe1-5 – anxiety, depression, somatic symptoms and life threatening events and number of pain sites at baseline; d1 – disturbance term for number of pain sites; R^2 = variance explained in number of pain sites

c) Model 2 Controlling for baseline pain

Controlling for the effects of a variable involves assessing the extent of a relationship between a predictor and an outcome by removing the influence of the third variable. The controlling for baseline pain model (example Figure 4.6) thus examines the number of pain sites at follow up that was predicted by baseline psychological stress, when accounting for baseline pain (along with confounding variables). This model also allows for the covariance between baseline psychological stress and baseline number of pain sites. This approach has been consistently used to assess the predictors of pain in prospective studies (Kamaleri et al, 2009; Holm et al, 2007).

Figure 4.6 Model 2 Controlling for baseline pain



PSe1-4 – error terms for anxiety, depression, somatic symptoms and life threatening events; d1 – disturbance term for number of pain sites; R^2 = variance explained in number of pain sites

One objective of the prospective analysis is to assess whether psychological stress at baseline predicts the number of pain sites at follow up. Models 1, 'pain as a stressor' and 2, 'controlling for baseline pain' were evaluated to identify the model that best explained the data. The RMSEA, SRMR and AIC model fit statistics were used to identify the most appropriate model for the GPSS data. The model selected was then used for the subsequent moderation, mediation and moderated mediation analysis using the GPSS data (see Chapter 7) and also in the analysis of the NorStOP dataset (see Chapter 10).

4.7 Chapter summary

This chapter described the statistical techniques used to address the aims and objectives outlined in Chapter 3. The distributions of the data were assessed by the Kolmogorov-Smirnov statistic with Lilliefors' significance test, to identify the appropriate statistical tests for the comparisons between participants and non-participants and for the descriptive analysis. The results of this analysis are presented in Chapter 6 for the GPSS study and Chapter 9 for NorStOP. Data missing completely at random testing and assessments were carried out and, where missing, data was imputed using estimation maximisation. Full imputed data was then used in the SEM analysis to test the trauma diathesis stress model of widespread pain. The results of this analysis are presented in Chapter 7 for the GPSS study and Chapter 10 for NorStOP.

Chapter 5 The General Practice Symptom Survey: Method

5.1 Chapter overview

As described in the aims and objectives in Chapter 3 (pg 78), the aim of the research detailed in this thesis was to identify whether individuals with a history of trauma have an increased susceptibility to widespread pain when they experience psychological stress. The moderation effect of childhood abuse on the relationship between psychological stress and widespread pain was assessed both cross-sectionally and prospectively using data from the General Practice Symptom Survey (GPSS). This chapter describes the methodology of the GPSS study, including the study design, procedure, sampling frame and the study questionnaire. I was not involved in the design or development of the questionnaire, nor was I involved in the data collection activity. This was all completed prior to my involvement with the study. However, I did determine which of the collected data items were relevant to my study (as detailed in Section 5.4) and how those data items would be used to test the trauma diathesis stress model of widespread pain, as described in Section 5.5 of this chapter.

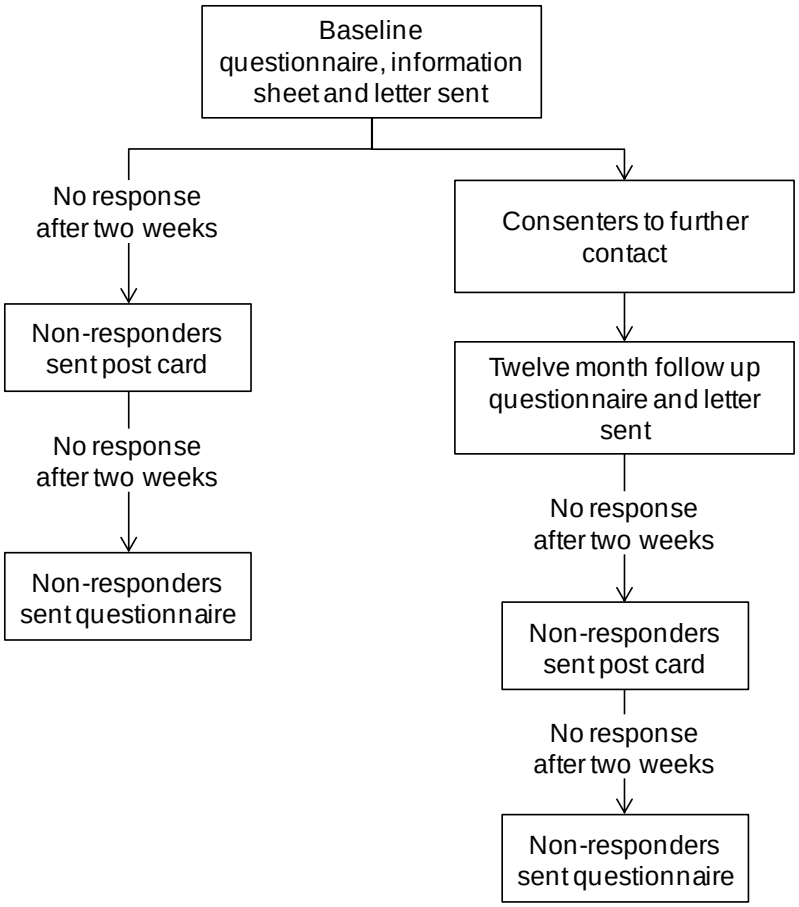
5.2 GPSS study design and procedure

The GPSS was a population based longitudinal postal survey. This epidemiological study was conducted to examine the development, persistence and co-existence of chronic fatigue syndrome, irritable bowel syndrome and chronic widespread pain in the general population. The study questionnaire (see Appendix 2) contained a set of validated measures designed to collect demographic details and information relating to pain, childhood abuse, psychological and social factors.

The study was conducted in two phases, with baseline questionnaires being mailed in April 2006 and follow up questionnaires being mailed in April 2007. A letter accompanying the questionnaire explained the purpose of the study and encouraged participation. At each phase, non-responders were sent a reminder postcard after two

weeks and a further questionnaire was sent after two more weeks, where necessary (Figure 5.1). The baseline questionnaire contained a section asking if responders could be contacted again. Only those specifically stating that they were happy to be contacted further were sent the follow up questionnaire.

Figure 5.1 Flowchart for GPSS mailing process



One element of the original GPSS study was to assess the impact of the length of the questionnaire on response rates. To assess this, two versions of the questionnaire were developed and issued at baseline. A long version contained all of the measures, with three measures omitted from a short version (see Section 5.4 below for more details). All participants received the same follow up questionnaire.

The study received ethical approval from the North Manchester Local Research Ethics Committee (REC reference number: 06/Q1406/14).

5.3 GPSS sampling frame

The population sampling frame of the GPSS study was the registered population of two general practices (GP) in North West England. Practice A is located in an area which has a population of 11,948, with a population density of 48.8 people per hectare. Practice B is located in an area which has a population of 4,530, with a population density of 1.11. The index of multiple deprivation combines information relating to employment, health, education, income, housing, services and crime. The index is then used to rank England's 32,482 lower super output areas (LSOA). The rank of index of multiple deprivation score for the area around practice A is 9,737 compared to 31,631 for practice B (rank ranges from one, most deprived, to 32,482, least deprived) (ONS, 2007). Using simple random sampling, 2,985 adults aged between 25 and 65 were selected from the registered populations of these two general practices.

5.4 GPSS study questionnaire

The GPSS survey contained a number of self-completion measures. Measures utilised in the current study (Table 5.1) are described in detail below, including a brief outline of their reliability and validity.

Table 5.1 Measures included in the baseline GPSS survey

Concept	Measure
Demographic details	
Bodily Pain	Body Manikin
Anxiety, depression	Hospital Anxiety and Depression Scale (HADS)
Somatic symptoms	Somatic Symptom Inventory (SSI)
Life threatening events	List of Life Threatening Events (LTE)
Childhood abuse	Childhood Physical and Sexual Abuse Questionnaire (CPSAQ)
Childhood neglect	Parental Bonding Instrument (PBI)
Social support	Single item question
Adult attachment style	Relationship Questionnaire (RQ)
Health anxiety*	Whitely Index (WI)
Somatosensory amplification*	Somatosensory Amplification Scale (SAS)
Dissociative experiences*	Dissociative Experiences Scale-Taxon (DES-T)

* These measures were excluded from the "short" version of the GPSS baseline survey.

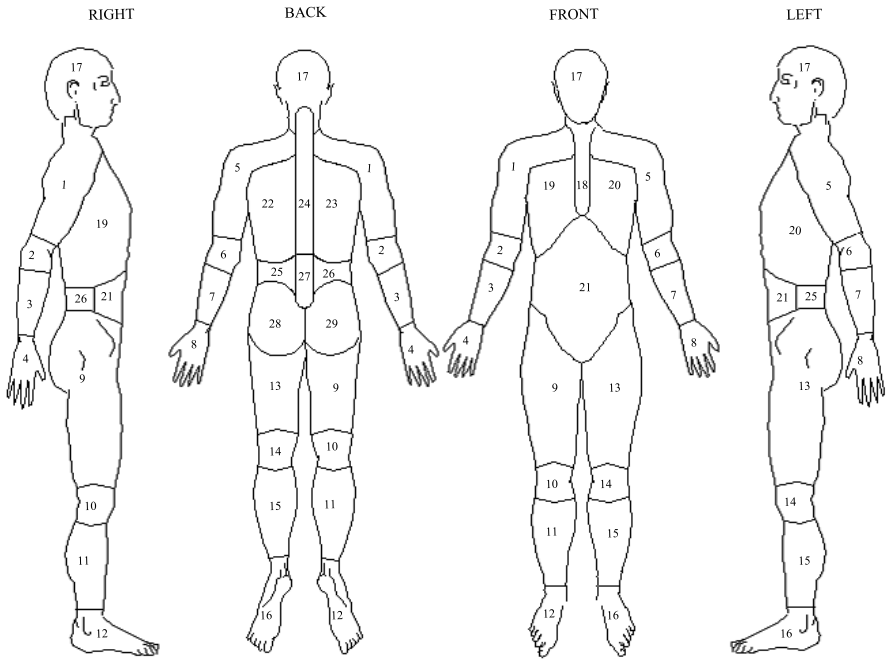
5.4.1 Demographic details

Demographic details including sex, date of birth, marital status, employment status and education were collected. Three groups were used to represent marital status: single; married (including cohabiting); and separated (including divorced or widowed), whilst employment status was classified into four categories: employed (including working full time, part-time, full time in the home); unemployed but seeking work; not working because of ill health; and other (including student, semi-retired or retired). Education was dichotomised based on whether the highest level of education or training was completed up to or after 16 years of age.

5.4.2 Assessment of pain

In both the baseline and follow up surveys, participants were asked “During the past month have you had any ache or pain which has lasted for one day or longer?” Those who responded positively were requested to indicate the location of their pain on four blank body manikins depicting the right, back, front and left sides of the body. Participants’ shading was subsequently coded using a template dividing the body into 29 sites, as shown in figure 5.2. This provided a count of pain sites from zero to 29 at both baseline and 12 month follow up. This method is routinely used in research using questionnaires to ascertain pain distribution and has been shown to have face validity (van den Hoven et al, 2010), good interrater reliability (product moment correlation coefficient r=0.99 Margolis et al, 1986; interclass correlation coefficient r =0.99 Lacey et al, 2005) and test-retest reliability of (product moment correlation coefficient) r=0.85 (Margolis et al, 1988).

Figure 5.2 GPSS Pain manikin 29 pain sites



5.4.3 Assessment of childhood abuse

Physical, emotional and sexual abuse was measured using the Childhood Physical and Sexual Abuse Questionnaire (CPSAQ) (Anderson et al, 1993). Neglect was assessed using the maternal care scale of the Parental Bonding Instrument (PBI - Parker et al, 1979).

Childhood physical and sexual abuse questionnaire

The CPSAQ (Anderson et al, 1993) is a self-report measure of the occurrence and frequency of physical, emotional and sexual abuse experienced before the participant was 17 years old. Physical abuse was assessed by two questions; did an adult or older person “hit, kick or beat you?” or “seriously threaten your life?” Participants were asked to respond never, seldom, occasionally or often. This resulted in a physical abuse score ranging from zero (a never response to both questions) to six (an often response to both questions). For emotional abuse, participants were asked to respond never, seldom, occasionally or often to one question concerning being insulted, humiliated or made to feel guilty by an adult or older person. This resulted in an emotional abuse score ranging from zero (a never response) to three (an often response). Sexual abuse was assessed

by five questions related to being touched, being made to touch, attempted or completed intercourse and other unwanted sexual contact or non-contact activities, by an adult or older person. Participants were asked to respond never, once, several times or often. This resulted in a sexual abuse score ranging from zero (a never response to all questions) to fifteen (an often response to all five questions).

Currently, there is no gold standard for assessing a history of childhood abuse (Widom et al, 2005). Methods of ascertaining a history of abuse within research include the use of documented records, which may under represent cases as discussed in Section 2.2.2a (pg22) and two self-report methods (interviews and questionnaires). Both self-report methods have their benefits. For example, interviews have the benefit of enabling the development of rapport between participant and researcher which can facilitate disclosure and also allows for clarification of definitions to assist recall (Martin et al, 1993). Questionnaires, on the other hand, offer the advantage of being time and cost efficient, and the "anonymity of a written response" may have a positive influence on disclosure (Martin et al, 1993, pg 389). The CPSAQ has been shown to have 70% agreement with the structured abuse interview (Leserman et al, 1996), 80% agreement with the Present State Examination (Martin et al, 1993) and has good test-retest reliability (77%) (Leserman et al, 1996).

Parental Bonding Instrument

The maternal care scale of the PBI (Parker et al, 1979) contains seven statements concerning the individual's recollection of maternal care during their first 16 years of life, for example "she spoke to me in a warm friendly voice". Each statement is rated as "Very like", "Moderately like", "Moderately unlike", "Very unlike'", scoring from 0 – 3, giving a range from 0 - 21. A higher score indicates greater maternal care. A cut-off point of less than or equal to 10 has been shown to identify neglect when compared to the Childhood Experience of Care and Abuse interview (sensitivity 79%, specificity 74% - Lancaster et al, 2007). The PBI has been shown to be stable over time; with a test retest

reliability of r=0.73 over 20 years (product moment correlation coefficient) (Wilhelm et al, 2004) and to be unaffected by current mood state (Parker et al, 1990).

5.4.4 Assessment of psychological stress

Psychological stress was assessed using the Hospital Anxiety and Depression Scale (HADS), the Somatic Symptoms Inventory (SSI) and the List of Threatening Events (LTE).

Hospital Anxiety and Depression Scale

The HADS (Zigmond & Snaith, 1983) assesses anxiety and depressive symptoms experienced in the previous week. Each of the two dimensions (anxiety and depression) has seven statements, to which the participant selects from four responses scored from 0 to 3. For example “I feel tense and wound up” requires a response from “most of the time” (3) to “not at all” (0). These responses are summed to give separate scores ranging from 0 – 21 for anxiety and depression. HADS avoids the physical items related to anxiety and depression that are included in other scales assessing anxiety and depression (Herrmann, 1997). This focus on the psychological symptoms of anxiety and depression make this measure appropriate for the current study assessing the relationship between psychological stress and number of pain sites.

Both the anxiety and depression scales have a six week test re-test reliability of r=0.70 (correlation) (Herrmann, 1997), internal consistency (Cronbach’s alpha mean 0.83 and 0.82 respectively) (Bjelland et al, 2002) and high sensitivity and specificity (0.80) when compared to clinical interviews (Bjelland et al, 2002; Olsson et al, 2005). The mean scores obtained from a UK general (non-clinical) population sample were 6.1 (standard deviation 3.8, median 6) for anxiety and 3.7 (standard deviation 3.1, median 3) for depression (Crawford et al, 2001).

Somatic Symptom Inventory

The SSI (Barsky et al, 1990a) assesses an individual's experience, in the past six months, of eleven symptoms taken from the Hopkins Symptom Checklist somatisation subscale (Derogatis et al, 1974) and two symptoms from the Minnesota Multiphasic Personality Inventory hypochondriasis subscale (Butcher et al, 1990). Participants rate how much they have been "bothered" by symptoms reflecting "psychological distress" (Derogatis et al, 1983, pg596). The inventory includes such symptoms as nausea, feeling fatigued, and a ringing or buzzing in the ears, which the participant rates on a five point scale from not at all (1) to a great deal (5). This gives a score ranging from 13 to 65, with higher scores indicating greater somatisation.

The 26 item version of the SSI has been shown to have test re-test reliability (product-moment correlation r=0.86) (Barsky et al, 1990a), interscale and internal consistency (Cronbach's alpha 0.95 and 0.89 respectively) (Barsky et al, 1990a; Waldinger et al, 2006). The scale also correlates strongly (r=0.74) with the clinician administered primary care evaluation of mental disorders interview and the diagnostic interview schedule for identifying somatisation disorder (Kroenke et al, 1998; Barsky et al, 2005). Mean scores on the 26 item questionnaire range from 36.7 for general non-clinical populations to 40.3 for insomnia patients (Hammad et al, 2001).

List of Threatening Events

Recent life events were measured using the LTE (Brugha et al, 1985). This questionnaire was developed from a semi-structured interview by Brown and Harris (1978) and the 67 item life event inventory of Tennant and Andrews (1977). Whilst the Brown and Harris (1978) interview is considered the gold standard for obtaining life event information, it is both time consuming and costly to administer and analyse the obtained data. Questionnaires, such as the LTE, are less time consuming to complete (increasing participation) and easier to interpret (increasing practicability) (Brugha et al, 1985).

The LTE asks participants if any of 12 threatening experiences or events have occurred within the previous 6 months. These include a serious illness or injury, having something valuable lost or stolen or being sacked from a job. Each question requires a yes or no response, with positive replies scoring 1, giving a range of 0 to 12. Higher scores indicate a greater number of threatening experiences. The LTE has been shown to have reasonable test-retest reliability of r=0.61 (Pearson's correlation coefficient) (Rosmalen et al, 2012), good agreement with semi-structured interviews (kappa 0.9) (Brugha & Cragg, 1990) and good agreement with interview and questionnaire responses from relatives (kappa 0.83 and 0.84, respectively) (Brugha & Cragg, 1990).

5.4.5 Potential mediators

Adult attachment style

Adult attachment style was assessed using the Relationship Questionnaire (RQ) (Bartholomew & Horowitz, 1991). Four basic styles of attachment have been identified (Bartholomew & Horowitz, 1991). Individuals with a secure attachment feel themselves to be worthy of care, and trust that others will be accepting and responsive. Secure attachments are the result of consistent responsive early caregiving (Ciechanowski et al, 2001). A dismissing attachment style, characterised by a negative view of others but a positive view of the self, often results from the consistent emotional unresponsiveness of the caregiver and leads an individual to become self-sufficient. Conversely, inconsistent emotional responsiveness can lead to a pre-occupied attachment style, in which individuals view themselves negatively (i.e. as not being worthy of care) but view others positively. Individuals with this style often strive for acceptance from others. Finally, individuals with the fearful style have a negative view of themselves and others as a result of constant criticism or rejection of the caregiver.

The RQ presents four statements, one representing each of the attachment styles. For example, "It is easy for me to become emotionally close to others. I am comfortable depending on them and having them depend on me. I don't worry about being alone or

having others not accept me" represents a secure attachment. Participants indicate the extent to which each statement describes their attitudes and feeling about relationships with others (from 1 "Not like me at all" to 7 "Very much like me"). This results in a score ranging from 1 to 7 for each attachment style. The RQ has been shown to have acceptable test-retest reliability (correlation r=0.7) (Sibley et al, 2005) and to have 92% agreement with semi-structured interviews (Bartholomew et al, 1991).

Social support

Social support was assessed using a single question, "Do you have someone with whom to discuss personal problems or turn to in a time of crisis?" A participant responding positively to this question was classified as having social support. Individuals who indicate that they have social support have been found to have reduced risk of physical health problems (Dickens et al, 2004).

Health anxiety

Health anxiety or hypochondriasis is defined as "a persistent preoccupation with disease despite reassurance given after thorough medical examination" (Pilowsky 1967, pg90). Health anxiety was measured using the Whitely Index (WI) (Pilowsky, 1967). This measure contains 14 items asking participants about their attitudes to their own health, for example "Do you worry a lot about your health?" and "Is it hard for you to believe the doctor when he / she tells you there is nothing for you to worry about?" Participants are asked to respond on a 5 point scale "not at all" (1) to "a great deal" (6). Scores range from 14 to 70, with higher scores indicating greater anxiety regarding health.

The WI has been shown to have internal consistency for medical outpatients, general practice and the general population (Cronbach's alpha 0.80, 0.78, 0.76, respectively) and test-retest reliability in medical outpatients (correlation r=0.90) (Speckens et al, 1996a). The scale has a sensitivity of 71-90% and specificity of 61-82% compared to the gold

standard of a structured interview using the Diagnostic and Statistical Manual of Mental Disorders III-R criteria for hypochondriasis (Speckens et al, 1996b).

Somatosensory amplification

Whilst the SSI assesses the recent experience of somatic symptoms, the Somatosensory Amplification Scale (SAS) (Barsky et al, 1990b) was designed to assess the extent to which normal physiological sensations and symptoms of organic disease are enhanced by heightened awareness. Participants rate 10 items, such as "I am often aware of various things happening within my body" and "I can sometimes hear my pulse or heartbeat throbbing in my ear" from 0 (Not at all) to 4 (Extremely). This results in a score ranging from 0 to 40 with higher scores indicating higher symptom amplification.

The SAS has a sensitivity of 52-58% and specificity of 40-60% compared to the gold standard of a structured interview using the Diagnostic and Statistical Manual of Mental Disorders III-R criteria for hypochondriasis (Speckens et al, 1996b). The SAS has been shown to have internal consistency for medical outpatients, general practice and the general population (Cronbach's alpha 0.77, 0.64, 0.71, respectively) and test-retest reliability in medical outpatients (correlation r=0.87) (Speckens et al, 1996a).

Dissociation

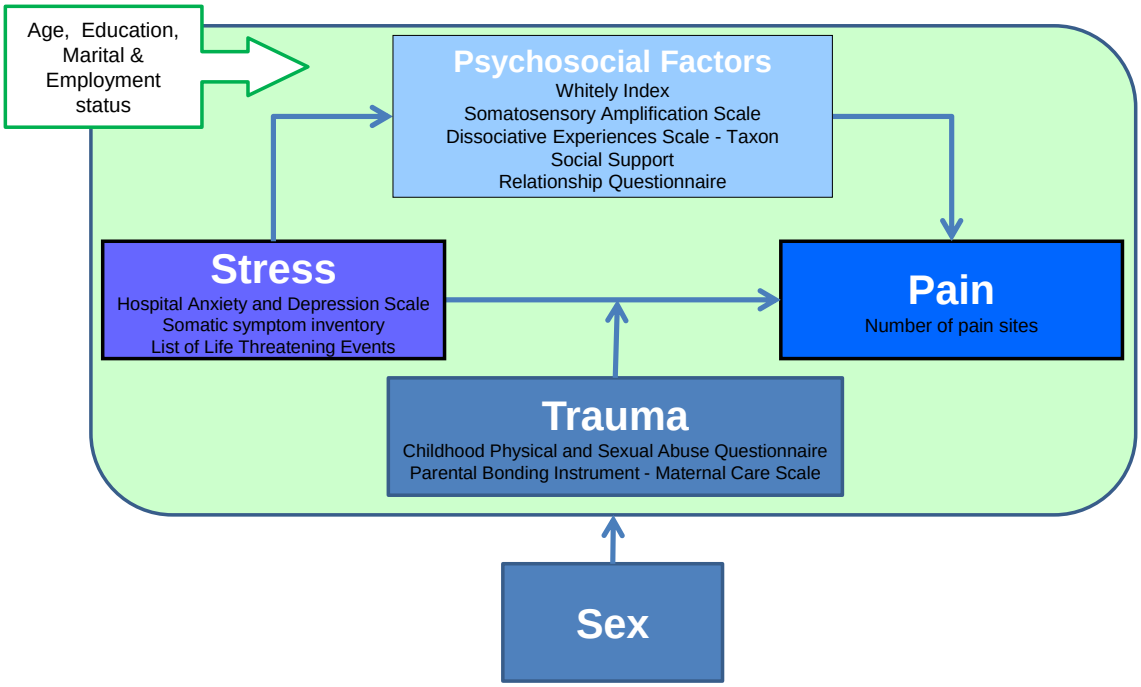
Dissociation has been defined as "partial or total disconnection between memories of the past, awareness of identity and of immediate sensations, and control of bodily movements often resulting from traumatic experiences, intolerable problems, or disturbed relationships" (Bob, 2008, pg10). The Dissociative Experiences Scale – Taxon (DES-T) (Waller et al, 1996) was adapted from the original 28 item Dissociative Experiences Scale (DES) (Bernstein & Putnam, 1986). The DES-T is better able to distinguish non-pathological dissociation (e.g. absorption) from pathological dissociation, such as amnesia and depersonalisation (Modestin & Erini, 2004). The DES-T contains eight statements such as "Some people have the experience of feeling that their body

does not belong to them." Participants are required to indicate the percentage of time they have each experience. This gives a score of 0 to 800 (Lang et al, 2004). Scores on the DES-T are strongly correlated with scores on the original DES measure in clinical and non-clinical populations (r=0.85 and 0.75 respectively) (Modestin & Erini, 2004). The DES-T has internal consistency (Cronbach's alpha 0.85) (Modestin & Erini, 2004) and 71.4% sensitivity in identifying dissociative disorders when compared to the gold standard of the Present State Examination (Lambert et al, 2001). The original DES has test-retest reliability correlations ranging from 0.78 to 0.93 (van Ijzendoorn & Schvergle, 1996).

5.5 Statistical analysis and data

The information collected from the above measures was used to compare participants and non-participants and in descriptive analysis as described in Sections 4.3 (pg79) and 4.4 (pg80) respectively. The following section describes how this data was used to test the childhood abuse diathesis stress model of widespread pain using SEM, as described in Section 4.6 (pg81). Figure 5.3 shows how the measures described above map onto the childhood abuse diathesis stress model of widespread pain. This is followed by a description of the outcome, predictor, confounding, moderator and mediator variables, which are then summarised in Table 5.2.

Figure 5.3 Mapping the measures onto the childhood abuse diathesis stress model of widespread pain



Note – the Whitely Index, Somatosensory Amplification Scale and Dissociative Experiences Scale – Taxon were only included in the "long" version of the GPSS baseline survey.

Outcome variables:

For the cross-sectional analysis the outcome was the number of pain sites at baseline. The number of pain sites at follow up was the outcome for the prospective analysis.

Predictor variable:

Confirmatory factor analysis was used to construct a latent variable *psychological stress* by assessing the common variance amongst the observed measures of anxiety, depression, somatic symptoms and life threatening events at baseline. In support of this approach, a recent review by Kopp et al (2010) regarding the measurement of psychological stress found that many current measures include the consideration of stressors, such as life event inventories, in addition to items which measure levels of psychological distress, including anxiety, depression and somatisation. Whilst it could be argued that other psychological and / or social factors could also have been integrated as measures of psychological stress, the theory and research evidence relating to these factors were more suggestive of their mediation effects.

Confounding variables:

Those demographic variables found to have a significant relationship with the number of pain sites in bivariate analysis were simultaneously added into the stress pain model. Only those variables having a significant relationship with the number of pain sites within the SEM model were retained.

Moderator variables:

Childhood abuse and neglect: Analysis was performed to assess whether the stress pain relationship was moderated by a particular type of childhood abuse or by the experience of any abuse or neglect. The impact of the extent of abuse was also assessed using a latent variable, as described below:

a) **Childhood abuse types:** Participants were classed as experiencing physical abuse if they responded seldom, occasionally or often to either of the two physical abuse questions. In the same way, participants were classed as experiencing emotional abuse if they responded seldom, occasionally or often to the emotional abuse question. Participants who responded once, several times or often to any of the five sexual abuse questions were classed as experiencing sexual abuse. The scores on the maternal scare scale of the PBI were transformed such that a score of zero indicated no neglect, with scores from one to eleven indicating greater levels of neglect. Participants scoring one or more on this scale were classified as having experienced childhood neglect. The four dichotomised variables, physical, emotional and sexual abuse and neglect, were used in both the bivariate analysis and as moderators in the SEM analysis.

b) **Any childhood abuse or neglect:** A participant was classed as experiencing any childhood abuse or neglect if they satisfied the criteria for any of the three abuse types (physical, emotional or sexual) or were assessed as being neglected. This

dichotomised variable was used in both the bivariate analysis and as a moderator in the SEM analysis.

c) Childhood abuse type score: Total scores for each of the four abuse type were calculated for each participant using the scores from the CSPAQ and the reversed and transformed neglect scores from the maternal care scale of the PBI. These four variables were used to create the *childhood abuse* latent variable. As described above (Section 5.4.3), this resulted in scores ranging from zero to six for childhood physical abuse, from zero to three for childhood emotional abuse, from zero to 15 for childhood sexual abuse and from zero to 11 for childhood neglect.

d) Childhood abuse latent variable: As described in Section 2.2.2a (pg22), the co-occurrence of abuse types is very common (Klott, 2013; Bernstein et al, 2003). Analysis of the individual types of abuse could result in each 'no abuse' group containing individuals who had experienced abuse of a different kind. Also, information regarding the frequency of abuse was lost by dichotomising the abuse variables into yes and no responses. In order to assess the impact of multiple types of, and the frequency of childhood abuse and neglect, a latent variable was created using the physical, emotional and sexual abuse scores from the CSPAQ and the reversed and transformed neglect scores from the maternal care scale of the parental bonding instrument. Using their scores on this latent variable, participants were categorised into three groups; 1) no abuse, 2) abuse, and 3) frequent abuse. Groups two and three were created by dichotomising the scores at the median point for those experiencing abuse. These three groups were then used in multiple group analysis (as described in Section 4.6.3, pg88) to assess the moderation effect of childhood abuse and neglect on the stress pain relationship.

Mediator variables:

The mediation of the stress pain relationship by adult attachment style, health anxiety, somatosensory amplification and dissociation was assessed using the total scores from each of the individual measures described above. The mediation effect of social support was examined using the dichotomous measure of social support.

Table 5.2 Summary of outcome, predictor, confounding, moderating and mediating variables for GPSS analysis

Type	Item	Measure	Range / categories
Outcome	Number of pain sites	Pain manikin	0 – 29
Predictor	*Psychological stress* latent variable	HADS / SSI / LTE	
Confounders	Age		25 – 65
	Marital status		Single, married, separated
	Employment status		Employed, unemployed, ill, other
	Education beyond 16		Yes / No
Moderators	Sex		Male, Female
	Childhood physical abuse	CPSAQ	Yes / No
	Childhood emotional abuse	CPSAQ	Yes / No
	Childhood sexual abuse	CPSAQ	Yes / No
	Childhood neglect	PBI-MC	Yes / No
	Any abuse or neglect	CPSAQ / PBI-MC	Yes / No
	Childhood abuse latent variable	CPSAQ / PBI-MC	No abuse, abuse, frequent abuse
Mediator	Secure attachment	RQ	1 – 7
	Fearful attachment	RQ	1 – 7
	Preoccupied attachment	RQ	1 – 7
	Dismissing attachment	RQ	1 – 7
	Social support		Yes / No
	Health anxiety	WI	14 – 70
	Somatosensory amplification	SAS	0 – 40
	Dissociation	DES-T	0 – 800

HADS = Hospital Anxiety and Depression Scale; SSI = Somatic Symptom Inventory, LTE = List of Life Threatening Events; CPSAQ = Childhood Physical and Sexual Abuse Questionnaire; PBI-MC = Parental Bonding Instrument maternal care scale; RQ = Relationship Questionnaire; WI = Whitely Index; SAS = Somatosensory Amplification Scale; DES-T = Dissociative Experiences Scale – Taxon.

5.6 Chapter summary

This chapter details the methodology of the GPSS study. Data relating to pain, childhood abuse and adult psychosocial factors were collected from a population based sample of males and females at baseline and 12 month follow up. The details of how this data was used to assess the trauma diathesis stress model of widespread pain were also provided. The results of the comparison between participants and non-participants are presented in chapter 6, whilst the results of the descriptive and SEM analysis are presented in chapter 7.

Chapter 6 The GPSS study: Comparison of participants and non-participants

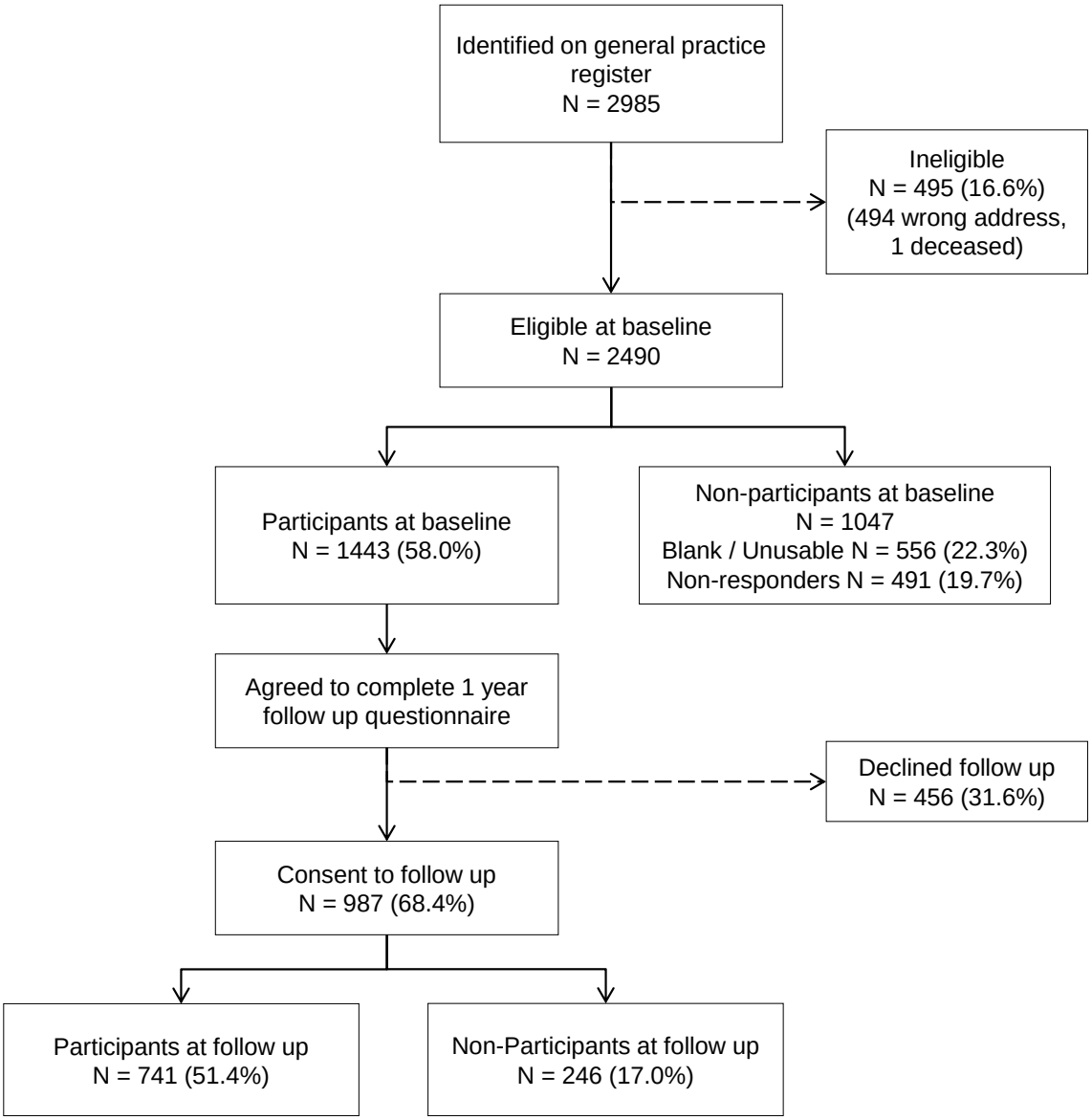
6.1 Chapter overview

This chapter describes the differences between participants and non-participants to the General Practice Symptom Survey (GPSS) in order to identify potential sources of response bias. Issues of bias are then discussed in terms of the implications for both the cross-sectional and prospective analyses of the GPSS data carried out in Chapter 7.

6.2 Participants and non-participants at baseline

Of the 2,985 individuals identified from the general practice registers, 495 (16.6%) were found to be ineligible (the address on the register did not match the electoral roll for 494 (16.5%) individuals and one person died before the study began). Of the resulting 2,490 eligible individuals who were sent the baseline questionnaire, 491 (19.7%) failed to respond and 556 (22.2%) returned questionnaires that were blank or did not contain useable information. This resulted in a study population of 1,443 participants (see Figure 6.1). At baseline 961 (66.6%) individuals completed the long version of the questionnaire and 482 (33.4%) completed the short version.

Figure 6.1 Participants and non-participants in the GPSS survey



Kolmogorov-Smirnov data distribution normality testing indicated non-normality for all variables; therefore non-parametric tests were used for all bivariate analysis.

Results of the comparisons between participants and non-participants at baseline show that the 1,443 participants were significantly more likely to be females and older than the 1,047 non-participants (Table 6.1). Further testing showed no significant difference in response rates between the two general practices or between the two different versions of the questionnaire (Table 6.1).

Table 6.1 Characteristics of participants and non-participants at baseline

	Participants (N=1,443)		Non-participants (N=1,047)		P
	median	IQR	median	IQR	
Age	47	38 – 57	43	34 – 54	**<0.001**[1]
	N	%	N	%	
Male	611	52.4	556	47.6	**<0.001**[2]
Female	832	62.9	491	37.1	
Practice A	631	56.3	490	43.7	0.128[2]
Practice B	812	59.3	557	40.7	
Long Questionnaire	961	58.0	696	42.0	0.949[2]
Short Questionnaire	482	57.9	351	42.1	

IQR = interquartile range; N = number; [1]Mann Whitney U test; [2]Chi squared test; significant differences in **red bold**

6.3 Participants and non-participants at follow up

Of the 1,443 participants completing the baseline questionnaire, 987 (68%) gave permission to be contacted again. The follow up questionnaire 12 months later was completed by 741 (51.5%) participants, 489 (66%) who completed the long version of the baseline questionnaire and 252 (34%) who had completed the short version of the baseline questionnaire, as shown in Figure 6.1. Of the remaining 702 participants at baseline, 456 (31.6%) failed to provide consent for further contact and 246 (17.0%) of those providing consent did not return the follow up questionnaire.

Comparisons between the 741 participants and 246 non-participants at follow up show that the non-participants were more likely to be younger and single (Table 6.2). Non-participants were also more likely to be working and have continued their education beyond age 16. Non-participants also reported higher levels of anxiety, depression and somatic symptoms at baseline than participants. There was no difference between participants and non-participants with regard to sex, social support, life threatening events, health anxiety, somatosensory amplification, dissociation, attachment style, the prevalence of childhood physical, emotional, sexual abuse or neglect or the number of pain sites.

Table 6.2 Characteristics of participants and non-participants at follow up

	Participants (N=741)			Non-participants (N=246)			P
	Total	N	%	Total	N	%	
Sex	741			246			
Male		309	76.0		98	24.0	0.607[1]
Female		432	74.5		148	25.5	
Marital Status	739			240			
Single		93	62.4		56	37.6	**<0.001**[2]
Married		572	78.6		156	21.4	
Separated		74	72.5		28	27.5	
Employment Status	732			239			
Employed		572	73.3		208	26.7	**0.003**[2]
Unemployed		13	72.2		5	27.8	
Not working as ill		20	69.0		9	31.0	
Other		127	88.1		17	11.8	
Education	727			238			**0.045**[1]
Up to age 16		207	79.9		52	20.1	
Post age 16		520	73.7		186	26.3	
Social Support	739			244			0.476[1]
Yes		694	75.4		226	24.6	
No		45	71.4		18	28.6	
Childhood physical abuse	738			244			0.059[1]
Yes		227	71.4		91	28.6	
No		511	77.0		153	23.0	
Childhood emotional abuse	736			243			0.272[1]
Yes		259	73.2		95	26.8	
No		477	76.3		148	28.7	
Childhood sexual abuse	738			242			0.283[1]
Yes		107	71.8		42	28.2	
No		631	75.9		200	24.1	
Childhood neglect	717			238			0.895[1]
Yes		111	75.5		36	24.4	
No		606	75.0		202	25.0	
Any abuse or neglect	726			243			0.568[1]
Yes		394	74.2		137	25.8	
No		332	75.8		106	24.2	
	N	**Median**	**IQR**	**N**	**Median**	**IQR**	**P**[3]
Age	741	50	40 – 58	246	40	33 – 50	**<0.001**
Anxiety	732	6	3 – 8	238	6	4 – 10	**0.001**
Depression	737	2	1 – 5	242	3	1 – 5	**0.020**
Somatic symptoms	720	20	16 – 24	237	21	17 – 26	**0.028**
Life threatening events	731	0	0 – 1	235	1	0 – 1	0.079
Secure attachment	729	4	3 – 6	240	4	2 – 6	0.108
Fearful attachment	724	2	1 – 4	240	2	1 – 4	0.298
Preoccupied attachment	720	2	1 – 3	239	2	1 – 2.5	0.490
Dismissing attachment	723	3	2 – 4	240	4	2 – 5	0.252
Health anxiety	475	20	17 – 25	154	20	17 – 26	0.361
Somatosensory amplification	480	9	6 – 13	161	10	6 – 15	0.125
Dissociation	486	20	0 – 40	162	20	0 – 60	0.526
NPS baseline	735	1	0 – 5	240	2	0 – 5.8	0.717

NPS baseline = Number of pain sites at baseline; IQR = interquartile range; N = number; [1] Chi squared test; [2]Kruskal Wallis test; [3]Mann Whitney U test; significant differences in **red bold**

6.4 Discussion

The GPSS study is a population based longitudinal postal survey of adults aged 25 to 65 years of age. 1,443 (58.0%) participants returned completed questionnaires at baseline, and 741 (51%) of those also responded to the follow up questionnaire twelve months later. A comparison was made between participants and non-participants at baseline and participants and non-participants at follow up in order to assess for potential response bias. Response bias can result in the incorrect assessment of associations between factors within the study population (internal validity) and also the overall generalisability (external validity) of these findings to the general population (Delgado-Rodrıguez & Llorca, 2004). These potential issues are addressed in turn.

Participants and non-participants at baseline

At baseline, data allowed for comparisons between participants and non-participants with regard to age, sex, general practice and the version of the questionnaire received (long or short). Participants at baseline were more likely to be female and older than non-participants. Although this is consistent with previous research (for example, Natvig et al, 2001; Gupta et al 2007; Bruusgaard et al, 2012), this under-representation of young males must be considered in the interpretation of study findings. As the research outlined in Section 1.4.1 (pg8) shows a higher prevalence of widespread pain in older females, the under-representation of young males may lead to an over estimate of the prevalence of widespread pain in the current study. However, the aim of this study was not to estimate the prevalence of widespread pain, but to assess its relationships with psychological stress and the moderation effect of trauma. Response bias would thus be introduced if there was a difference in the relationship between the predictor (psychological stress) and the outcome (widespread pain) between participants and non-participants. This then becomes a question of whether the association between psychological stress and widespread pain varies with age or between males and females. Both of these factors were considered within the analysis models: age, as a confounding variable and sex, as a moderator (see Sections 7.5 and 7.6), and the results are discussed in Section 7.7 and

11.6. Another potential source of bias could be the differences in response due to the use of short and long questionnaires. Previous research has shown that shorter questionnaires achieve higher response rates (Edwards et al, 2002). However, this was not the case in the GPSS study. There was no difference between response rates to the long and short versions of the questionnaire.

It is also possible that the sensitive nature of the questions relating to childhood abuse may have deterred some individuals from participating in the study. For example, individuals with an experience of severely traumatic childhood abuse may have failed to respond to avoid painful memories, thus reducing any effects seen. On the other hand, individuals who had not experienced abuse may have failed to respond as they felt the study was not relevant to them (Walker et al, 1999). However, this is less likely as the childhood abuse measure formed only a small section at the end of the questionnaire pack. Although it is difficult to assess the impact of such sensitive questions, the fact that the rate of missing data was low (see Section 7.4) and the overall response rate (58.0%) to the survey was similar to other population based postal surveys (e.g. Kamaleri et al, 2008b 54.4%; Carnes et al, 2007 60%) suggest that this was not an issue.

Participants and non-participants at follow up

Comparisons were made between participants and non-participants at follow up based on all data collected at baseline. Although there was a significant difference in the response rate between males and females at baseline, this was not the case at follow up. Of the 407 males who were eligible for follow up, 309 (76%) participated, whilst 432 (75%) of the females participated. No difference was found with regard to childhood abuse or the number of pain sites reported at baseline. However, consistent with previous research, non-participants had reported higher levels of anxiety, depression and somatisation at baseline than participants (Jones et al, 2011; Volken, 2013). It is possible that the relationship between these predictor variables (anxiety, depression and somatisation) and widespread pain would be different in those who did not participate at

follow up. This could lead to an underestimation of any association between these variables and widespread pain. However, inspection of the differences between those who participated and those who did not are small (Table 6.2) and hence the likely effect would be minimal.

6.5 Chapter summary

This chapter has presented and discussed the differences between participants and non-participants to the GPSS baseline and 12 month follow up survey. When considering the external validity, or generalisability of the study findings, it must be noted that young males were under-represented in the baseline survey and that the participants in the follow up survey were also more likely to be older. Descriptive and inferential analysis of this data is presented in the following chapter.

Chapter 7 The GPSS study: Results – childhood trauma, stress and pain

7.1 Chapter overview

This chapter presents the findings from the analysis of the General Practice Symptom Survey (GPSS) data. An assessment was made of the associations between the number of pain sites and demographic factors, anxiety, depression, somatic symptoms, life threatening events, social support, adult attachment style, health anxiety, somatosensory amplification and dissociation. Prevalence of childhood abuse and neglect within the study population is also presented. Structural Equation Modelling (SEM) was used to examine the trauma diathesis stress model of widespread pain both cross-sectionally and prospectively and the results are presented in Sections 7.5 and 7.6, respectively. The final section of this chapter provides a discussion regarding these findings, including the strengths and limitations of the study and the implications for the trauma diathesis stress model of widespread pain.

7.2 Participant characteristics and association with baseline number of pain sites

This section provides a summary of the characteristics of the 1,443 participants who responded to the baseline GPSS survey.

7.2.1 Number of pain sites

Pain site information was reported by 1,418 (98.3%) participants. The number of pain sites ranged from 0 to the maximum of 29, with a median of 1 (inter quartile range 0 – 5). No pain was reported by 673 (47.5%) participants, with only one participant reporting pain in all 29 sites.

7.2.2 Association between number of pain sites at baseline and covariates

As shown in Table 7.1, the number of pain sites was significantly higher for those participants who were separated, divorced or widowed, not working due to ill health, those who had not pursued education beyond age 16 years and those without social support. There was no difference in the number of pain sites between males and females.

Table 7.1 Characteristics of participants by number of pain sites at baseline

Item	Total	N	%	Pain Sites at baseline		
				Median	IQR	P
Sex	1,418					0.834[1]
Male		602	42.5	1	0 – 5	
Female		816	57.5	1	0 – 5	
Marital Status	1,402					**0.001**[2]
Single		221	15.8	0	0-4	
Married		1,043	74.4	1	0-5	
Separated		138	9.8	3	0-8	
Employment Status	1,393					**<0.001**[2]
Working		1,116	80.1	1	0-5	
Unemployed		25	1.8	3	0-9	
Not working as ill		36	2.6	7.5	3-14.3	
Other		216	15.5	1	0-5	
Education	1,376					**<0.001**[1]
Up to age 16		382	27.8	2	0-6	
Post age 16		994	72.2	1	0-4	
Social Support	1,435					**0.032**[1]
Yes		1,334	93.0	1	0-5	
No		101	7.0	2	0-9	
Childhood physical abuse	1,409					**0.005**[1]
Yes		435	30.9	2	0-5	
No		974	69.1	1	0-5	
Childhood emotional abuse	1,407					**<0.001**[1]
Yes		485	34.5	2	0-6	
No		922	65.5	0	0-4	
Childhood sexual abuse	1,408					0.165[1]
Yes		199	14.1	1	0-5	
No		1,209	85.9	1	0-5	
Childhood neglect	1,368					0.077[1]
Yes		190	13.9	2	0-6	
No		1,178	86.1	1	0-5	
Any childhood abuse or neglect	1,389					**<0.001**[1]
Yes		724	52.1	2	0-6	
No		665	47.9	0	0-4	

Total = Total number of participants responding to items; IQR = inter quartile range, [1]Mann-Whitney U Tests; [2]Kruskall-Wallis test; significant differences in **red bold**

Childhood physical, emotional and sexual abuse was reported by 442 (31%), 489 (34%) and 201 (14%) participants, respectively. Childhood neglect was reported by 192 (14%) participants. There was no significant difference in the prevalence of childhood abuse or neglect with regard to age ($p=0.111$) and no sex difference in the overall reporting of childhood abuse and neglect (males 54%, females 50%, $p=0.130$). However, there were significant differences when the individual types of abuse were assessed separately. Males were significantly more likely than females to report childhood physical (37% vs 27%; $p<0.001$) and emotional abuse (39% vs 30%; $p=0.001$), whilst females were significantly more likely than males to report childhood sexual abuse (17% vs 10%; $p<0.001$) and neglect (16% vs 11%; $p=0.010$). Of the 734 participants reporting any form of abuse or neglect, 330 (45%) reported one type of abuse or neglect, 247 (34%) reported two types, 128 (17%) reported three types and 29 (4%) reported experiencing all four types of abuse. When considering the individual types of childhood abuse, the number of pain sites was significantly higher for participants reporting physical and emotional abuse but not sexual abuse or neglect. The number of pain sites was also significantly higher for participants reporting any childhood abuse or neglect compared to those participants reporting no such history (Table 7.1).

The median age of the participants was 47 (interquartile range 38-57), with males (median 48, IQR 39 – 58) being significantly older than the females (median 46, IQR 36 – 57, $p=0.031$). There were significant correlations between many of the factors included in this analysis (Table 7.2). For example, significant positive correlations were found between the number of pain sites and age, anxiety, depression, somatic symptoms and life threatening events, fearful and dismissing attachment styles, health anxiety, somatosensory amplification, dissociation, and childhood physical, emotional and sexual abuse. A significant negative correlation was found between the number of pain sites and secure attachment style (Table 7.2). Significant positive correlations were found between anxiety, depression, somatic symptoms and life threatening events and between the four types of childhood abuse. Childhood physical and emotional abuse

and neglect were significantly associated with all other factors, whilst childhood sexual abuse was only significantly associated with anxiety, depression, somatic symptoms and life threatening events, fearful and preoccupied attachment style and dissociation.

Table 7.2 Pearson correlations between anxiety, depression, somatic symptoms, life threatening events, attachment style, health anxiety, somatosensory amplification, dissociation, childhood abuse, age and number of pain sites at baseline

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. HADS-A	1															
2. HADS-D	**0.641****	1														
3. SSI	**0.531****	**0.566****	1													
4. LTE	**0.254****	**0.318****	**0.301****	1												
5. Secure	**-0.218****	**-0.278****	**-0.148****	-0.051	1											
6. Fear	**0.331****	**0.377****	**0.261****	**0.156****	**-0.427****	1										
7. Preocc	**0.261****	**0.264****	**0.190****	**0.119****	**-0.174****	**0.364****	1									
8. Dismiss	-0.001	**0.091****	**0.061***	0.038	**-0.212****	**0.222****	**0.056***	1								
9. HA	**0.497****	**0.507****	**0.587****	**0.257****	**-0.158****	**0.266****	**0.156****	**0.084***	1							
10. SAS	**0.306****	**0.240****	**0.414****	**0.181****	-0.064	**0.228****	**0.113****	**0.068***	**0.465****	1						
11. DES-T	**0.328****	**0.281****	**0.289****	**0.184****	**-0.070***	**0.231****	**0.225****	**0.093****	**0.225****	**0.200****	1					
12. CPA	**0.172****	**0.192****	**0.205****	**0.216****	**-0.059***	**0.138****	**0.082****	**0.059***	**0.191****	**0.160****	**0.156****	1				
13. CEA	**0.264****	**0.255****	**0.250****	**0.201****	**-0.112****	**0.224****	**0.132****	**0.083****	**0.206****	**0.147****	**0.231****	**0.619****	1			
14. CSA	**0.129****	**0.098****	**0.129****	**0.079****	-0.047	**0.086****	**0.097****	0.026	0.056	0.050	**0.284****	**0.319****	**0.311****	1		
15. CN	**0.159****	**0.190****	**0.135****	**0.069***	**-0.141****	**0.208****	**0.108****	**0.057***	**0.093****	0.054	**0.101****	**0.332****	**0.338****	**0.209****	1	
16. Age	**-0.172****	-0.029	0.006	-0.027	-0.018	**-0.089****	**-0.068***	0.025	0.004	0.021	**-0.120****	-0.012	-0.035	-0.044	-0.006	1
17. NPS B	**0.275****	**0.360****	**0.525****	**0.218****	**-0.081****	**0.095****	0.040	**0.055***	**0.397****	**0.175****	**0.169****	**0.131****	**0.152****	**0.089****	0.045	**0.053***

Significant correlations in **red bold**; **correlation is significant at the 0.01 level (2-tailed); *correlation is significant at the 0.05 level (2-tailed); HADS-A = Anxiety; HADS-D = Depression; SSI = Somatic symptoms; LTE = Threatening life events; Secure = Secure attachment; Fear = Fearful attachment; Dismiss = Dismissing attachment; Preocc = Preoccupied attachment; HA = Health anxiety; SAS = Somatosensory amplification; DES-T = Dissociation; CPA = Childhood physical abuse sum of score from two questions from the CPSAQ; CEA = Childhood emotional abuse score from one question from the CPSAQ; CSA = Childhood sexual abuse sum of score on five questions from the CPSAQ; CN = Childhood neglect score transformed from maternal care scale of the PBI; NPS B = Number of pain sites at baseline

7.3 Participant characteristics and association with follow up number of pain sites

This section provides a summary of the characteristics of the 741 participants who responded to the GPSS survey at one year follow up.

7.3.1 Number of pain sites at follow up

The number of pain sites, reported by 737 (99.5%) participants, ranged from 0 to 25, with a median of 1 (inter quartile range 0 – 4). Only one participant reported pain in 25 sites and 336 (45.6%) participants reported no pain. Compared to baseline, 371 (50.3%) participants had pain in the same number of sites plus or minus one pain site; 233 (31.6%) participants had pain in fewer sites, 272 (36.9%) had pain in the same number of sites and 232 (31.5%) reported pain in more sites at follow up. Of the 673 participants reporting no pain at baseline, 339 (50.4%) completed the follow up survey and 222 (65.5%) of those continued to report no pain at follow up.

7.3.2 Association between number of pain sites at follow up and covariates

As shown in Table 7.3, the number of pain sites at follow up was significantly higher for those participants who were separated, divorced or widowed, were unemployed, had not pursued education beyond age 16 years and those reporting childhood physical and emotional abuse. There was no difference between males and females in the number of pain sites or with regard to age (median 50, IQR 40 – 58, p=0.499). .

The significant associations between the number of pain sites at baseline and social support and any childhood abuse or neglect were no longer found when considering the number of pain sites at follow up.

Table 7.3 Characteristics of participants by number of pain sites at follow up

Item	Total*	N	%	Pain Sites at follow up Median	IQR	P
Sex	737					0.423[1]
Male		308	41.8	1	0 – 4	
Female		429	58.2	1	0 – 4	
Marital Status	735					**<0.001[2]**
Single		92	12.5	0	0 – 3	
Married		569	77.4	1	0 – 4	
Separated		74	10.1	3	0 – 8.3	
Employment Status	728					**<0.001[2]**
Working		568	78.0	1	0 – 4	
Unemployed		13	1.8	0	0 – 9.5	
Not working as ill		20	2.7	8	4.3 – 13.3	
Other		127	17.5	2	0 – 5	
Education	723					**<0.001[1]**
Up to age 16		207	28.6	2	0 – 6	
Post age 16		516	71.4	1	0 – 4	
Social Support	735					0.064[1]
Yes		690	93.9	1	0 – 4	
No		45	6.1	2	0 – 8	
Childhood physical abuse	734					**0.038[1]**
Yes		225	30.7	2	0 – 6	
No		509	69.3	1	0 – 4	
Childhood emotional abuse	732					**0.040[1]**
Yes		259	35.4	2	0 – 5	
No		473	64.6	1	0 – 4	
Childhood sexual abuse	734					0.304[1]
Yes		107	14.6	1	0 – 5	
No		627	85.4	1	0 – 4	
Childhood neglect	713					0.080[1]
Yes		110	15.4	2	0 – 5	
No		603	84.6	1	0 – 4	
Any childhood abuse or neglect	722					0.167[1]
Yes		392	54.3	1	0 – 5	
No		330	45.7	1	0 – 4	

*Total number of participants responding to items; IQR = inter quartile range, [1]Mann-Whitney U Tests; [2]Kruskall-Wallis test; significant differences in **red bold**

Significant positive correlations were found between the number of pain sites at follow up and age, anxiety, depression, somatic symptoms and life threatening events, fearful attachment style, health anxiety, somatosensory amplification, dissociation, childhood physical and emotional abuse, childhood neglect and number of pain sites at baseline (Table 7.4). Significant positive correlations were also found between anxiety, depression, somatic symptoms and life threatening events and between the four types of

childhood abuse. Childhood physical abuse was significantly associated with all other factors. No associations were found between childhood emotional and dismissing attachment style, between sexual abuse and secure, preoccupied, dismissing attachment styles and somatosensory amplification, or between neglect and life threatening events, health anxiety and somatosensory amplification.

Table 7.4 Pearson correlations between anxiety, depression, somatic symptoms, life threatening events, attachment style, health anxiety, somatosensory amplification, dissociation, childhood abuse, number of pain sites at baseline and number of pain sites at follow up

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. HADS-A	1																
2. HADS-D	**0.643****	1															
3. SSI	**0.483****	**0.584****	1														
4. LTE	**0.264****	**0.377****	**0.291****	1													
5. Secure	**-0.261****	**-0.287****	**-0.155****	-0.060	1												
6. Fear	**0.341****	**0.401****	**0.271****	**0.146****	**-0.470****	1											
7. Preocc	**0.261****	**0.292****	**0.229****	**0.122****	**-0.228****	**0.353****	1										
8. Dismiss	0.012	**0.096***	0.057	**0.084***	**-0.258****	**0.260****	0.019	1									
9. HA	**0.491****	**0.525****	**0.573****	**0.235****	**-0.130****	**0.265****	**0.198****	0.090	1								
10. SAS	**0.303****	**0.231****	**0.388****	**0.163****	-0.066	**0.189****	0.058	0.029	**0.451****	1							
11. DES-T	**0.340****	**0.304****	**0.279****	**0.211****	**-0.094***	**0.199****	**0.149****	0.086	**0.256****	**0.195****	1						
12. CPA	**0.196****	**0.247****	**0.221****	**0.240****	**-0.083***	**0.190****	**0.154****	**0.074***	**0.167****	**0.182****	**0.209****	1					
13. CEA	**0.251****	**0.277****	**0.246****	**0.190****	**-0.141****	**0.240****	**0.147****	0.065	**0.168****	**0.152****	**0.223****	**0.606****	1				
14. CSA	**0.141****	**0.106****	**0.122****	**0.081***	-0.053	**0.102****	0.062	0.026	**0.098***	0.050	**0.362****	**0.224****	**0.275****	1			
15. CN	**0.109****	**0.147****	**0.111****	0.032	**-0.150****	**0.203****	**0.092***	**0.074***	-0.029	-0.050	**0.147****	**0.309****	**0.331****	**0.188****	1		
16. Age	**-0.169****	-0.021	0.036	-0.015	-0.006	-0.036	**-0.082***	0.034	0.012	0.084	**-0.092****	0.008	-0.006	0.036	0.004	1	
17. NPS B	**0.252****	**0.333****	**0.509****	**0.245****	**-0.089***	**0.117****	**0.086***	0.052	**0.338****	**0.169****	**0.197****	**0.113****	**0.133****	0.033	0.022	0.047	1
18. NPS F	**0.253****	**0.321****	**0.462****	**0.194****	-0.071	**0.095***	0.050	0.052	**0.314****	**0.200****	**0.193****	**0.131****	**0.140****	0.038	**0.084***	**0.083***	**0.564****

Significant correlations in **red bold**; **correlation is significant at the 0.01 level (2-tailed); *correlation is significant at the 0.05 level (2-tailed); HADS-A = Anxiety; HADS-D = Depression; SSI = Somatic symptoms; LTE = Threatening life events; Secure = Secure attachment; Fear = Fearful attachment; Dismiss = Dismissing attachment; Preocc = Preoccupied attachment; HA = Health anxiety; SAS = Somatosensory amplification; DES-T = Dissociation; CPA = Childhood physical abuse sum of score from two questions from the CPSAQ; CEA = Childhood emotional abuse score from one question from the CPSAQ; CSA = Childhood sexual abuse sum of score on five questions from the CPSAQ; CN = Childhood neglect score transformed from maternal care scale of the PBI; NPS B = Number of pain sites at baseline; NPS F – number of pain sites at follow up

7.4 Missing data

Although overall missing data was less than 5% per item (criteria for acceptability as discussed in Section 4.5) the accumulative effect of full case analysis would result in a 20% loss in sample size at baseline and 21% at follow up. As Little's MCAR test (see Section 4.5 for details) showed data to be missing completely at random, data was imputed for 295 participants. However, MCAR testing showed that health anxiety, somatosensory amplification and dissociation data was not missing completely at random. Mediation analysis using these variables was therefore restricted to full case. This resulted in a sample size of 906 and 468 participants for cross-sectional and prospective mediation analysis, respectively.

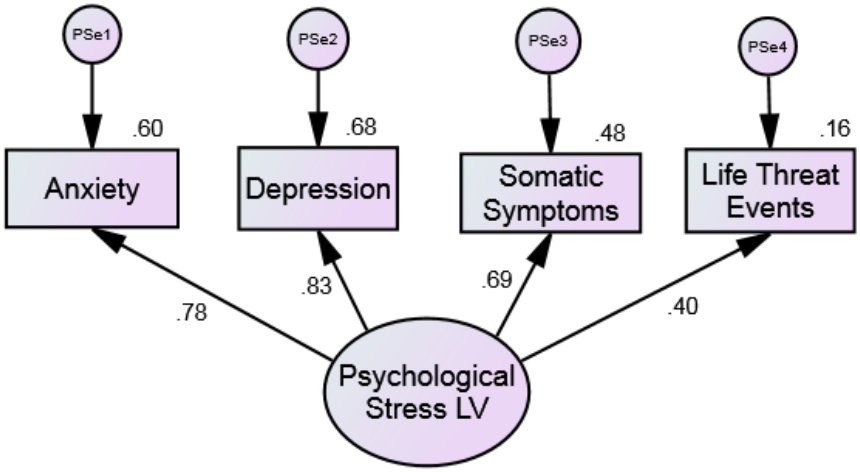
7.5 Cross-sectional structural equation modelling

These results are based on 1,443 baseline participants, including 295 participants with imputed data.

7.5.1 Stress and pain

The *psychological stress* latent variable (Figure 7.1) was a good fit to the data (RMSEA ≤0.06 and SRMR ≤0.09). Each of the observed measures had a statistically significant relationship with the *psychological stress* latent variable. Table 7.5 shows the standardised (β) and unstandardized regression (b) coefficients for the *psychological stress* latent variable.

Figure 7.1 Psychological stress latent variable



Root mean square error of approximation (RMSEA) = 0.055
Standardised root mean square residual (SRMR) = 0.017

PSe1-4 = error terms for anxiety, depression, somatic symptoms and threatening events; LV = latent variable; numbers on arrows from latent variable = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

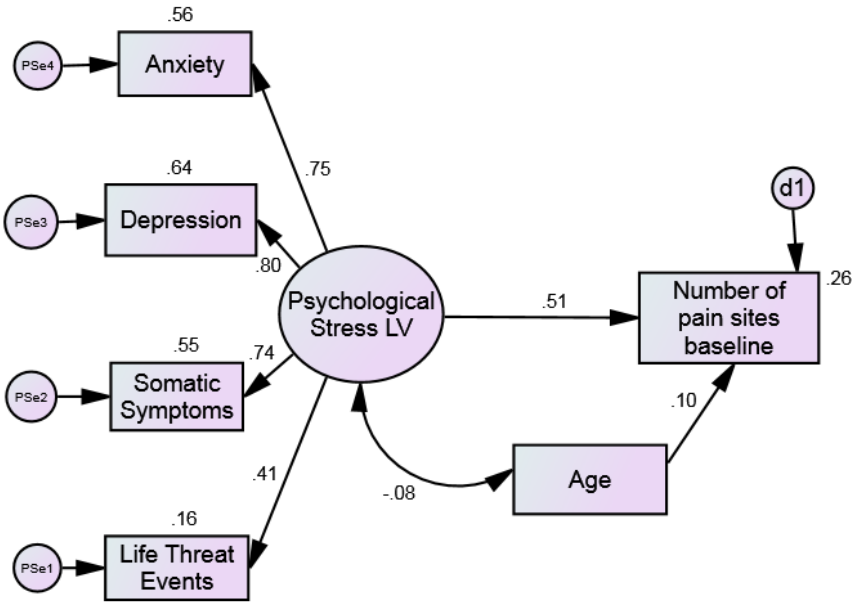
Table 7.5 Regression coefficients for psychological stress latent variable

Observed Variable	β	95% C.I.		B	95% C.I.		R^2
Anxiety	0.775	0.740	0.809	1.000	1.000	1.000	0.601
Depression	0.826	0.791	0.806	0.886	0.805	0.975	0.682
Somatic symptoms	0.691	0.641	0.735	1.517	1.360	1.688	0.477
Threatening events	0.395	0.326	0.464	0.165	0.131	0.199	0.156

β = Standardised regression coefficient; B = Unstandardised regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation

Based on previous research and the findings of significant associations with number of pain sites in the bivariate analysis (see Section 7.2.2 above), age, education, employment and marital status were considered as potential confounders of the stress pain relationship. The analysis showed no significant relationship between the number of pain sites and education (p = 0.105), employment (p = 0.938) or marital status (p = 0.083). Only age was found to have a significant contribution (p=0.005) and so was retained as a confounder in the final model (as shown in Figure 7.2). The *psychological stress* latent variable had a statistically significant relationship with the number of pain sites (β = 0.51, p<0.001). This model explains 26% of the variance in pain (Figure 7.2; Table 7.6).

Figure 7.2 Psychological stress and number of pain sites controlling for age



Root mean square error of approximation (RMSEA) = 0.040
Standardised root mean square residual (SRMR) = 0.0506

PSe1-4 = error terms for anxiety, depression, somatic symptoms and threatening events; d1 = disturbance term for number of pain sites; LV = latent variable; numbers on arrows = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

7.5.2 Stress and pain: moderation by childhood abuse

Using the model from Figure 7.2, the moderation effect of each individual type of abuse was tested separately. Table 7.6 shows the regression coefficients for the stress pain relationship firstly for all participants and then for each abuse type. The stress pain relationship was significantly stronger for individuals reporting childhood emotional abuse compared to those without such a history ($\beta = 0.57$, R^2 32% compared to $\beta = 0.45$, R^2 20%, $p<0.05$). The stress pain relationship was not significantly different when comparing individuals with and without childhood physical or sexual abuse or neglect.

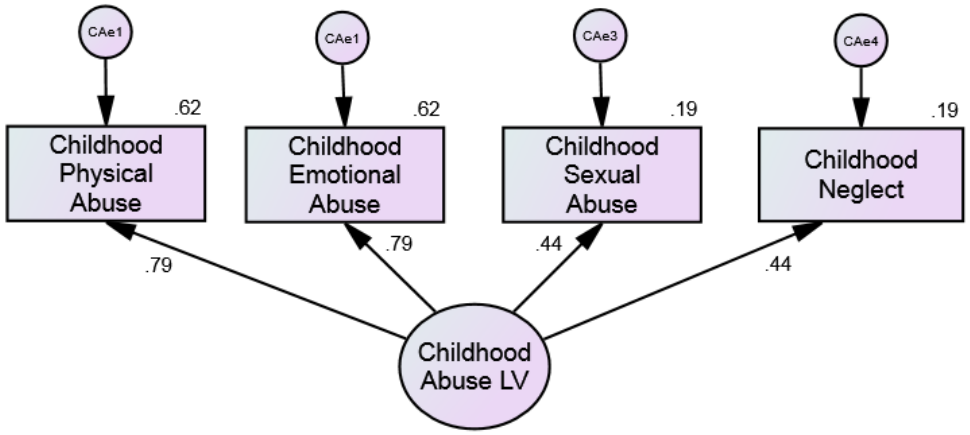
Table 7.6 Psychological stress and number of pain sites at baseline moderated by childhood abuse type

		N	%	β	95% CI		B	R^2	Comparison
All participants		1443		0.506	0.422	0.578	0.753	0.257	
Childhood abuse type									
Physical abuse	No	993	68.8	0.483	0.390	0.568	0.709	0.238	Referent
	Yes	450	31.2	0.536	0.382	0.683	0.844	0.285	-1.399
Emotional abuse	No	945	65.5	0.446	0.346	0.540	0.688	0.204	Referent
	Yes	498	34.5	0.567	0.435	0.683	0.876	0.317	**-1.980***
Sexual abuse	No	1240	85.9	0.512	0.424	0.587	0.769	0.267	Referent
	Yes	203	14.1	0.466	0.243	0.679	0.722	0.201	0.353
Neglect	No	1245	86.3	0.515	0.418	0.599	0.789	0.269	Referent
	Yes	198	13.7	0.475	0.315	0.633	0.707	0.218	0.636
Any abuse or neglect	No	702	48.6	0.451	0.324	0.567	0.657	0.213	Referent
	Yes	741	51.4	0.522	0.405	0.626	0.826	0.269	-1.884

β = Standardised regression coefficient for psychological stress to pain relationship; B = Unstandardised regression coefficient for psychological stress to pain relationship; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B; significant values in **red bold**; *p value <0.05

Due to the high level of co-occurrence between abuse types (Section 7.2.2) and significant positive correlations between the four abuse types (Table 7.2) a latent variable childhood abuse was constructed as shown in Figure 7.3. Each of the observed measures had a statistically significant relationship (p<0.001) with the *childhood abuse* latent variable, which was a good fit for the data. Table 7.7 shows the coefficients and confidence intervals for the *childhood abuse* latent variable.

Figure 7.3 Childhood abuse latent variable



Root mean square error of approximation (RMSEA) = 0.058
Standardised root mean square residual (SRMR) = 0.0209

CAe1-4 – error terms for childhood physical, emotional and sexual abuse and neglect; LV = latent variable; numbers on arrows from latent variable = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

Table 7.7 Regression coefficients for childhood abuse latent variable

Observed Variable	β	95% C.I.		B	95% C.I.		R^2
Childhood Physical Abuse	0.786	0.706	0.849	1.000	1	1	0.617
Childhood Emotional Abuse	0.787	0.731	0.861	0.916	0.771	1.131	0.619
Childhood Sexual Abuse	0.441	0.342	0.534	0.833	0.616	1.081	0.194
Childhood Neglect	0.436	0.351	0.523	1.004	0.783	1.259	0.190

β = Standardized regression coefficient; B = Unstandardized regression coefficient (factor loadings); 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation

Participants' scores on the *childhood abuse* latent variable were used to create three groups; group one comprised the 702 (48.7%) individuals reporting no abuse. Groups two and three were created by dichotomising the scores at the median point of those who indicated abuse. Group two "abuse" contained 406 (28.1%) participants and group three "frequent abuse" consisted of the 335 (23.2%) participants who reported experiencing more frequent abuse and / or multiple types of abuse. Mean scores for the *psychological stress* latent variable differed significantly for the no abuse, abuse and frequent abuse groups (-0.69, 0.09 and 1.34 respectively, $p<0.001$). The median number of pain sites for the no abuse, abuse and frequent abuse groups was 0 (0 – 4), 1 (0 – 5) and 2 (0 – 6) respectively ($p<0.001$).

These three groups were used to assess the moderation effect of childhood abuse on the stress pain relationship, again using the model depicted in Figure 7.2. As shown in Table 7.8, childhood abuse did moderate the stress pain relationship. The stress pain relationship was significant for all groups ($p<0.001$), and was significantly stronger ($p<0.05$) for the participants reporting frequent abuse compared to those reporting no abuse. There was also an increase in the variance in pain sites explained by the model, increasing from 21% for the no abused group to 33% for those who were frequently abused.

Table 7.8 Psychological stress and number of pain sites moderated by childhood abuse latent variable

Group	N	%	β	95% CI		B	R^2	Comparisons
All	1443		0.506	0.426	0.577	0.753	0.257	
No abuse	702	48.7	0.451	0.323	0.569	0.657	0.213	Referent
Abuse	406	28.1	0.450	0.299	0.592	0.808	0.201	1.229
Frequent abuse	335	23.2	0.573	0.431	0.699	0.869	0.334	**1.968***

β = Standardized regression coefficient; B = Unstandardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B; significant values in **red bold**; *p value <0.05

7.5.3 Stress and pain: moderation by childhood abuse and sex

The results in Table 7.1 show no significant difference between males and females with regard to the reported number of pain sites. However, mean scores on the *psychological stress* latent variable were significantly higher in females (0.1) than males (-0.1, $p = 0.046$). Pairwise comparison shows no significant difference in the strength of the stress pain relationship between males and females ($p>0.05$). For male participants, there was a significant difference ($p<0.05$) in the strength of the stress pain relationship between those individuals reporting no abuse ($\beta = 0.530$) and those reporting frequent abuse ($\beta = 0.664$ $p<0.05$, Table 7.9). For female participants, there was a significant difference ($p<0.02$) in the strength of the stress pain relationship between individuals

reporting no abuse (β = 0.367) and those reporting abuse (β = 0.561) but not frequent abuse (β = 0.501). The stress pain relationship was significant for all groups (p<0.001).

Table 7.9 Psychological stress and number of pain sites moderated by childhood abuse latent variable and sex

Group		N	%	β	β 95% CI		B	R^2	Comparisons
Males	All	611		0.523	0.397	0.633	0.795	0.272	
	No abuse	288	47.1	0.530	0.356	0.690	0.728	0.294	Referent
	Abuse	179	29.3	0.319	0.090	0.578	0.576	0.101	-0.864
	Frequent abuse	144	23.6	0.664	0.431	0.825	1.092	0.416	**2.137***
Females	All	832		0.489	0.388	0.580	0.716	0.243	
	No abuse	414	49.7	0.367	0.201	0.546	0.562	0.142	Referent
	Abuse	227	27.3	0.561	0.376	0.695	1.013	0.311	**2.569****
	Frequent abuse	191	23.0	0.501	0.315	0.671	0.720	0.279	1.102

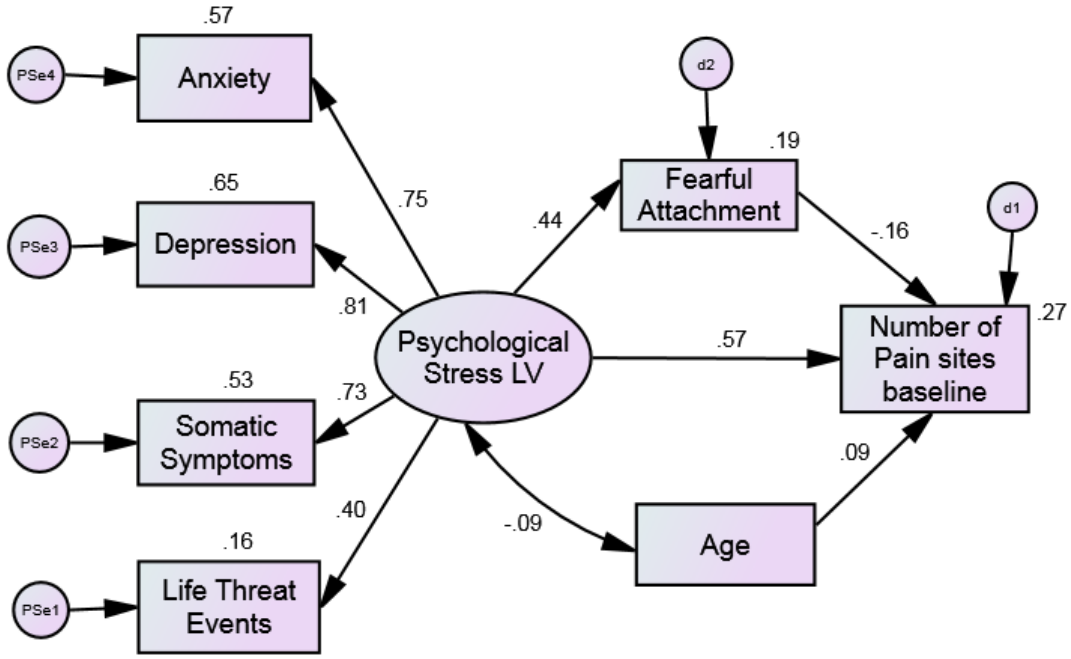
β = Standardized regression coefficient for psychological stress to pain relationship; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B; significant values in **red bold**; *p value <0.05; **p value <0.02

7.5.4 Stress and pain: Mediation by psychosocial factors

The trauma diathesis stress model of widespread pain proposed a number of psychological and social variables as potential pathways through which stress might influence widespread pain. This section presents the results of the mediation analysis for adult attachment style, social support, health anxiety, somatosensory amplification and dissociation.

Eight mediation models were created by adding each of the potential psychosocial mediators to the model depicted in Figure 7.2. Figure 7.4 shows an example of the resulting models, in which fearful attachment style mediates the stress pain relationship (indirect effect β = -0.070, p < 0.001, R^2 0.27).

Figure 7.4 Stress and pain sites mediated by fearful attachment style



Root mean square error of approximation (RMSEA) = 0.036
Standardised root mean square residual (SRMR) = 0.0486

PSe1-4 = error terms for anxiety, depression, somatic symptoms and threatening events; d1-2 = disturbance term for number of pain sites and fearful attachment style; LV = latent variable; numbers on arrows = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

The stress pain relationship was also mediated by secure attachment style and preoccupied attachment style. No mediation effect was found for dismissing attachment style, social support (Table 7.10), health anxiety, somatosensory amplification or dissociation (Table 7.11).

Table 7.10 Psychological stress and number of pain sites at baseline mediated by adult attachment style and social support

Mediator			β	95% CI		P	B	R^2	a	b
Attachment Style	Secure	Indirect	-0.022	-0.038	-0.010	**<0.001***	-0.030	0.258	-0.281	0.079
		Direct	0.522	0.443	0.598	0.001	0.776		(-0.339, -0.220)	(0.034, 0.124)
		Total	0.500	0.421	0.573	0.001	0.743			
	Dismissing	Indirect	0.001	-0.002	0.005	0.358	0.001	0.258	0.070	0.014
		Direct	0.505	0.424	0.579	0.001	0.753		(0.012, 0.129)	(-0.030, 0.056)
		Total	0.506	0.426	0.581	0.001	0.754			
	Fearful	Indirect	-0.070	-0.099	-0.047	**<0.001***	-0.104	0.272	0.438	-0.160
		Direct	0.571	0.487	0.650	0.001	0.849		(0.381, 0.492)	(-0.213, -0.112)
		Total	0.501	0.424	0.574	0.001	0.745			
	Preoccupied	Indirect	-0.053	-0.098	-0.025	**<0.001***	-0.095	0.215	0.328	-0.162
		Direct	0.492	0.338	0.619	0.001	0.875		(0.210, 0.441)	(-0.243, 0.088)
		Total	0.438	0.291	0.569	0.001	0.780			
Social Support		Indirect	-0.002	-0.016	0.011	0.711	-0.004	0.259	-0.209	0.011
		Direct	0.509	0.445	0.573	0.001	0.765		(-0.285, -0.132)	(-0.050, 0.069)
		Total	0.507	0.445	0.571	0.001	0.761			

Analysis based on 1,443 participants; β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical value $p < 0.05$; * Significant indirect effects in **red bold**

Table 7.11 Psychological stress and number of pain sites at baseline mediated by health anxiety, somatosensory amplification and dissociation

Mediator		β	95% CI		P	B	R^2	a	b
Health Anxiety	Indirect	0.000	-0.001	0.005	0.504	0.000	0.246	0.010	0.024
	Direct	0.494	0.392	0.587	0.001	0.732		(-0.055, 0.076)	(-0.030, 0.084)
	Total	0.494	0.392	0.588	0.001	0.732			
Somatosensory Amplification	Indirect	0.000	-0.004	0.004	0.922	0.000	0.245	-0.053	0.000
	Direct	0.494	0.393	0.589	0.001	0.732		(-0.126, 0.020)	(-0.054, 0.055)
	Total	0.494	0.393	0.589	0.001	0.732			
Dissociation	Indirect	0.000	-0.004	0.001	0.511	0.000	0.244	0.017	-0.015
	Direct	0.494	0.392	0.589	0.001	0.731		(-0.041, 0.080)	(-0.064, 0.043)
	Total	0.494	0.392	0.589	0.001	0.731			

Analysis based on 906 participants; β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical value $p < 0.05$; ***Significant indirect effects in **red bold**

7.5.5 Stress and pain: Moderated mediation

Each of the mediation models examined in the previous section were next assessed to identify any moderation effects of childhood abuse and sex.

a) Moderation by childhood abuse

The mediation of the stress pain relationship by secure, fearful and preoccupied attachment styles were moderated by abuse status. For secure attachment style, the indirect effects were significant in those individuals who had experienced frequent abuse (β=-0.03, p=0.001), but were not significant for those participants in the abuse and no abuse groups (abuse β=-0.02, p=0.099; no abuse β=-0.01, p=0.166; see Table 7.12). The indirect effects for fearful attachment style were significant for both the abuse groups (frequent abuse β=-0.07 p<0.001; abuse β=-0.05, p=0.001), but not for the no abuse group (no abuse β=-0.03, p=0.074; Table 7.13). The indirect effects for preoccupied attachment style were significant for both the abuse groups (frequent abuse β=-0.04 p<0.001; abuse β=-0.05, p=0.004), but not for the no abuse group after adjustment for multiple comparisons (no abuse β=-0.03, p=0.011; Table 7.14).

The stress pain relationship was not mediated by dismissing attachment style, social support, health anxiety, somatosensory amplification or dissociation, even when examining the no abuse, abuse and frequent abuse groups individually (Appendix 4 Tables 1 - 5).

b) Moderation by childhood abuse and sex

Secure attachment was a significant mediator of the stress pain relationship for males in both abuse groups (abuse β=-0.05, p=0.014; frequent abuse β=-0.05; p=0.027). For the female participants, the indirect effects for all three groups failed to reach significance (see Table 7.12). Similarly for males fearful attachment mediated the stress pain relationship in both abuse groups (abuse β=-0.08, p=0.007; frequent abuse β=-0.13, p=0.001). For females, however, the opposite result was found, with the indirect effects

for fearful attachment reaching significance only for the no abuse group (no abuse β=-0.05, p=0.004; Table 7.13). Preoccupied attachment style was a significant mediator for males in the abused group (abuse β=-0.06, p=0.028; Table 7.14), whilst the indirect effects were significant for all female participants, regardless of abuse status. However, when accounting for multiple comparisons (setting the critical value for p at 0.006 as described in Section 4.6.5, pg90) only the following indirect effects remained significant: fearful attachment style for males experiencing frequent abuse and fearful and preoccupied attachment styles for females not experiencing abuse.

The stress pain relationship was not mediated by dismissing attachment style, social support, health anxiety, somatosensory amplification or dissociation, even when examining the no abuse, abuse and frequent abuse groups individually by sex (Appendix 4 Tables 1 - 5).

Table 7.12 Psychological stress and number of pain sites at baseline mediated by secure attachment style and moderated by childhood abuse and sex

			β	β 95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.008	-0.024	0.003	0.166	-0.012	0.212	-0.187	0.044		
		Direct	0.456	0.333	0.573	0.001	0.665		(-0.267, 0.101)	(-0.024, 0.107)	RMSEA	0.035
		Total	0.447	0.324	0.563	0.001	0.653				SRMR	0.0489
	Abuse	Indirect	-0.017	-0.050	0.003	0.099	-0.031	0.197	-0.244	0.071		
		Direct	0.458	0.313	0.590	0.001	0.816		(-0.357, -0.133)	(-0.020, 0.167)		
		Total	0.440	0.296	0.581	0.001	0.785					
	Frequent Abuse	Indirect	-0.025	-0.047	-0.010	**<0.001***	-0.037	0.323	-0.374	0.067		
		Direct	0.584	0.448	0.713	0.001	0.874		(-0.491, -0.223)	(0.028, 0.109)		
		Total	0.559	0.423	0.693	0.001	0.837					
Males	No abuse	Indirect	-0.012	-0.042	0.008	0.241	-0.016	0.294	-0.224	0.052		
		Direct	0.538	0.359	0.699	<0.001	0.743		(-0.338, -0.114)	(-0.045, 0.150)		
		Total	0.527	0.352	0.688	<0.001	0.727					
	Abuse	Indirect	-0.045	-0.117	-0.008	0.014	-0.080	0.125	-0.274	0.163		
		Direct	0.362	0.130	0.606	0.003	0.651		(-0.447, -0.105)	(0.020, 0.306)		
		Total	0.318	0.097	0.564	0.005	0.571					
	Frequent Abuse	Indirect	-0.049	-0.150	-0.004	0.027	-0.081	0.433	-0.275	0.179		
		Direct	0.702	0.442	0.847	0.001	1.153		(-0.494, -0.011)	(0.026, 0.337)		
		Total	0.653	0.422	0.818	<0.001	1.072					
Females	No abuse	Indirect	-0.007	-0.029	0.006	0.263	-0.010	0.142	-0.161	0.040		
		Direct	0.370	0.201	0.548	0.001	0.568		(-0.276, -0.035)	(-0.048, 0.124)		
		Total	0.364	0.203	0.542	0.001	0.558					
	Abuse	Indirect	0.003	-0.029	0.032	0.811	0.005	0.298	-0.216	-0.013		
		Direct	0.546	0.357	0.691	0.001	0.972		(-0.371, -0.057)	(-0.138, 0.118)		
		Total	0.549	0.363	0.693	0.001	0.977					
	Frequent Abuse	Indirect	-0.026	-0.112	0.053	0.522	-0.036	0.271	-0.458	0.056		
		Direct	0.515	0.289	0.712	0.001	0.727		(-0.589, -0.307)	(-0.120, 0.217)		
		Total	0.490	0.307	0.652	0.001	0.691					

Analysis based on 1,443 participants: No abuse = 702, Abuse = 406, Frequent Abuse = 335. Males = 611: No abuse = 288, Abuse = 179, Frequent Abuse = 144. Females = 832: No abuse = 414, Abuse = 227, Frequent Abuse = 191. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006. *Significant indirect effects in **red bold**

Table 7.13 Psychological stress and number of pain sites at baseline mediated by fearful attachment style and moderated by childhood abuse and sex

			β	95% CI		P	B	R^2	a	b	Model Fit
All	No abuse	Indirect	-0.026	-0.059	0.003	0.074	-0.038	0.216	0.371	-0.071	
		Direct	0.477	0.345	0.598	0.001	0.689		(0.288, 0.445)	(-0.146, 0.009)	RMSEA 0.036
		Total	0.450	0.328	0.564	0.001	0.652				SRMR 0.0486
	Abuse	Indirect	-0.050	-0.100	-0.016	**0.001***	-0.089	0.207	0.350	-0.142	
		Direct	0.486	0.339	0.619	0.001	0.867		(0.235, 0.459)	(-0.233, -0.050)	
		Total	0.436	0.295	0.569	0.001	0.778				
	Frequent Abuse	Indirect	-0.068	-0.102	-0.040	**<0.001***	-0.101	0.339	0.436	-0.155	
		Direct	0.630	0.490	0.763	0.001	0.947		(0.306, 0.544)	(-0.214, -0.11)	
		Total	0.563	0.426	0.697	0.001	0.845				
Males	No abuse	Indirect	0.027	-0.026	0.077	0.291	0.036	0.298	0.419	0.064	
		Direct	0.504	0.310	0.673	0.001	0.691		(0.292, 0.525)	(-0.059, 0.191)	
		Total	0.531	0.355	0.69	<0.001	0.728				
	Abuse	Indirect	-0.076	-0.186	-0.018	0.007	-0.138	0.124	0.405	-0.188	
		Direct	0.385	0.155	0.616	0.002	0.697		(0.239, 0.566)	(-0.353, -0.05)	
		Total	0.309	0.104	0.531	0.003	0.559				
	Frequent Abuse	Indirect	-0.126	-0.286	-0.047	**0.001***	-0.212	0.504	0.394	-0.320	
		Direct	0.792	0.522	0.950	0.001	1.330		(0.173, 0.571)	(-0.516, -0.180)	
		Total	0.666	0.428	0.817	0.001	1.119				
Females	No abuse	Indirect	-0.054	-0.110	-0.017	**0.004***	-0.081	0.161	0.343	-0.156	
		Direct	0.420	0.233	0.593	0.001	0.636		(0.233, 0.454)	(-0.260, -0.049)	
		Total	0.366	0.201	0.536	0.001	0.555				
	Abuse	Indirect	-0.028	-0.093	0.005	0.096	-0.049	0.303	0.309	-0.09	
		Direct	0.574	0.396	0.714	0.001	1.020		(0.147, 0.451)	(-0.226, 0.030)	
		Total	0.547	0.365	0.685	0.001	0.970				
	Frequent Abuse	Indirect	-0.059	-0.161	0.014	0.125	-0.084	0.274	0.487	-0.121	
		Direct	0.548	0.325	0.756	0.001	0.778		(0.338, 0.613)	(-0.278, 0.039)	
		Total	0.489	0.304	0.652	0.001	0.694				

Analysis based on 1,443 participants: No abuse = 702, Abuse = 406, Frequent Abuse = 335. Males = 611: No abuse = 288, Abuse = 179, Frequent Abuse = 144. Females = 832: No abuse = 414, Abuse = 227, Frequent Abuse = 191. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006. *Significant indirect effects in **red bold**

Table 7.14 Psychological stress and number of pain sites at baseline mediated by preoccupied attachment style and moderated by childhood abuse and sex

			β	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.028	-0.057	-0.006	0.011	-0.041	0.223	0.295	-0.096		
		Direct	0.481	0.353	0.602	0.001	0.700		(0.211, 0.376)	(-0.169, -0.018)	RMSEA	0.037
		Total	0.453	0.329	0.57	0.001	0.659				SRMR	0.0610
	Abuse	Indirect	-0.049	-0.104	-0.016	**0.004***	-0.088	0.212	0.326	-0.151		
		Direct	0.487	0.330	0.618	0.001	0.866		(0.201, 0.445)	(-0.254, -0.058)		
		Total	0.438	0.283	0.570	0.001	0.778					
	Frequent Abuse	Indirect	-0.044	-0.083	-0.018	**<0.001***	-0.066	0.344	0.299	-0.147		
		Direct	0.612	0.469	0.736	0.001	0.915		(0.164, 0.412)	(-0.222, -0.078)		
		Total	0.568	0.425	0.695	0.001	0.849					
Males	No abuse	Indirect	-0.003	-0.038	0.031	0.884	-0.004	0.297	0.322	-0.010		
		Direct	0.536	0.346	0.695	0.001	0.738		(0.189, 0.444)	(-0.102, 0.101)		
		Total	0.533	0.189	0.689	0.001	0.734					
	Abuse	Indirect	-0.055	-0.145	-0.006	0.028	-0.101	0.118	0.360	-0.153		
		Direct	0.367	0.151	0.619	0.001	0.673		(0.191, 0.514)	(-0.314, -0.009)		
		Total	0.312	0.117	0.560	0.001	0.572					
	Frequent abuse	Indirect	-0.013	-0.097	0.006	0.202	-0.022	0.411	0.162	-0.083		
		Direct	0.669	0.434	0.831	0.001	1.086		(-0.032, 0.404)	(-0.262, 0.091)		
		Total	0.656	0.428	0.824	<0.001	1.065					
Females	No abuse	Indirect	-0.042	-0.090	-0.013	**0.004***	-0.064	0.162	0.277	-0.153		
		Direct	0.407	0.241	0.201	0.001	0.615		(0.166, 0.394)	(-0.253, -0.047)		
		Total	0.364	0.592	0.542	0.001	0.551					
	Abuse	Indirect	-0.045	-0.129	-0.002	0.028	-0.079	0.315	0.304	-0.148		
		Direct	0.591	0.393	0.728	0.001	1.036		(0.112, 0.476)	(-0.293, -0.009)		
		Total	0.546	0.349	0.682	0.001	0.957					
	Frequent abuse	Indirect	-0.076	-0.171	-0.015	0.012	-0.109	0.305	0.392	-0.195		
		Direct	0.573	0.332	0.759	0.001	0.820		(0.241, 0.528)	(-0.348, -0.038)		
		Total	0.497	0.301	0.658	0.001	0.711					

Analysis based on 1,443 participants: No abuse = 702, Abuse = 406, Frequent Abuse = 335. Males = 611: No abuse = 288, Abuse = 179, Frequent Abuse = 144. Females = 832: No abuse = 414, Abuse = 227, Frequent Abuse = 191. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006. *Significant indirect effects in **red bold**.

7.6 Prospective structural equation modelling

This section describes the examination of the trauma diathesis stress model of widespread pain using the predictors, mediators and moderators at baseline and the number of pain sites at 12 month follow up. These results are based on the 737 participants responding to the follow up survey. The analysis of the mediation effect of health anxiety, somatosensory amplification and dissociation was carried out for the subset of 468 participants completing the long version of the baseline GPSS survey.

7.6.1 Stress and pain

The cross-sectional analysis found that among adults, an increase in psychological stress was associated with a higher number of sites of pain. Prospective analysis was performed to assess whether psychological stress predicts widespread pain.

Two alternative prospective models were assessed for the best representation of the data. Both models adequately fit the data (see Table 7.15). The most appropriate was model 2 according to the criteria detailed in Section 4.6.6. This model, controlling for baseline pain, was therefore used in the subsequent analysis (Figure 7.5).

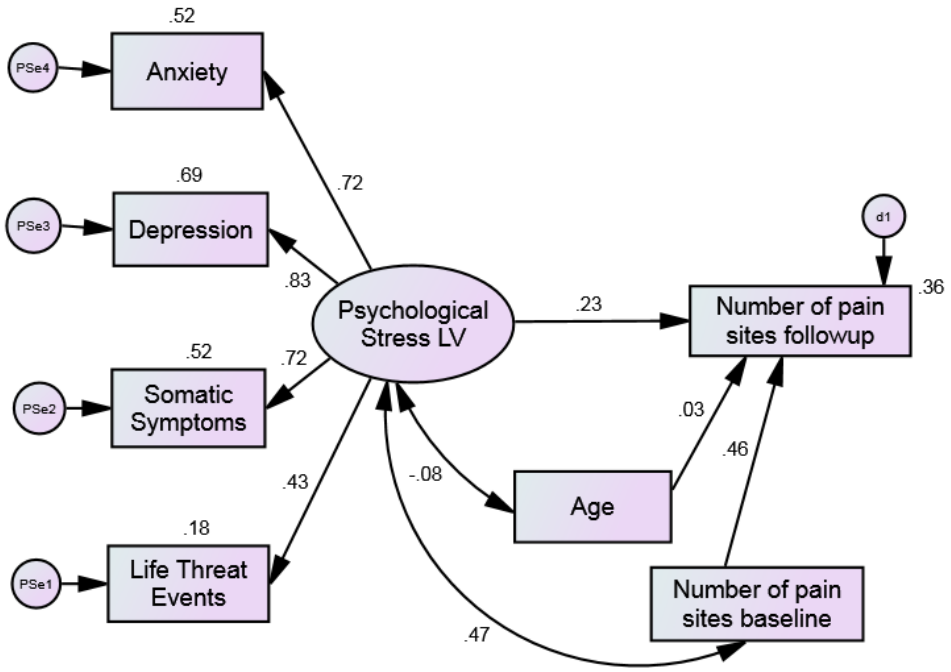
Table 7.15 Comparison of prospective models

Model	β	B	R^2	RMSEA	SRMR	AIC
1. Pain as a stressor	0.540	0.860	0.290	0.051	0.076	1345.045
2. Controlling for pain	0.229	0.333	0.359	0.041	0.055	823.449

β = Standardized regression coefficient; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; RMSEA = Root mean square error of approximation; SRMR = Standardised root mean square residual; AIC = Akaike information criterion

Psychological stress, measured by the baseline *psychological stress* latent variable, had a statistically significant relationship with the number of pain sites at follow up (β = 0.23, P<0.001) and explained 36% of the variance in the number of pain sites.

Figure 7.5 Model 2 Stress and pain: Controlling for pain



Root mean square error of approximation (RMSEA) = 0.041
Standardised root mean square residual (SRMR) = 0.055

PSe1-4 = error terms for anxiety, depression, somatic symptoms and threatening events; d1 = disturbance term for number of pain sites at follow up; LV = latent variable; numbers on arrows = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

7.6.2 Stress and pain: moderation by childhood abuse

The mean scores on the *psychological stress* latent variable for the no abuse, abuse and frequent abuse groups were -0.62, 0.04 and 1.20 respectively ($p<0.001$). The median number of pain sites (IQR) for the no abuse, abuse and frequent abuse groups was 1 (0 – 4), 1 (0 – 4) and 2 (0 – 6) respectively ($p=0.029$). Using the model from Figure 7.5 and the baseline *childhood abuse* latent variable, the strength of the stress pain relationship did not vary significantly between the three abuse groups (see Table 7.16). However, stress did not predict the number of pain sites at follow up for individuals who experienced frequent abuse ($p=0.170$).

Table 7.16 Psychological stress and number of pain sites at follow up moderated by childhood abuse latent variable

Group	N	%	β	95% CI		B	R^2	Comparisons
All	737		0.230	0.175	0.295	0.334	0.359	
No abuse	342	46.4%	0.287	0.152	0.429	0.443	0.368	Referent
Abuse	225	30.5%	0.317	0.129	0.538	0.533	0.335	0.545
Frequent abuse	170	23.1%	0.108	-0.036	0.263	0.159	0.401	-1.940

β = Standardized regression coefficient; B = Unstandardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B

7.6.3 Stress and pain: moderated by childhood abuse and sex

There was no significant difference between males and females with regard to the number of pain sites (Table 7.3) or mean scores on the *psychological stress* latent variable (females 0.1, males -0.1, p = 0.149). As shown in Table 7.17, there was no significant difference in the strength of the stress pain relationship between the three abuse groups for males or females. However, stress did not predict the number of pain sites at follow up for females who experienced abuse (p=0.080).

Table 7.17 Psychological stress and number of pain sites at follow up moderated by childhood abuse latent variable and sex

Group		N	%	β	β 95% CI		B	R^2	Comparisons
Males	All	330		0.236	0.176	0.310	0.334	0.312	
	No abuse	151	45.8%	0.368	0.135	0.595	0.521	0.262	Referent
	Abuse	102	30.9%	0.351	0.084	0.660	0.574	0.351	0.241
	Frequent abuse	77	23.3%	0.231	0.152	0.323	0.334	0.433	-1.267
Females	All	407		0.220	0.170	0.289	0.334	0.404	
	No abuse	191	46.9%	0.235	0.098	0.392	0.387	0.470	Referent
	Abuse	123	30.2%	0.221	-0.040	0.488	0.380	0.314	-0.026
	Frequent abuse	93	22.9%	0.189	0.124	0.290	0.334	0.402	-1.325

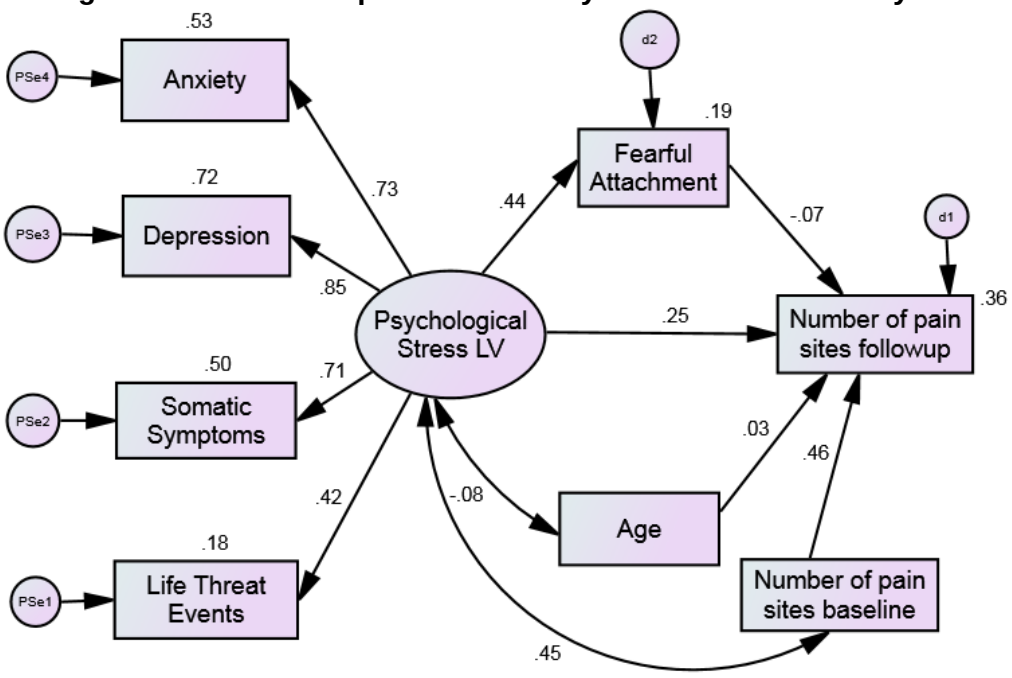
β = Standardized regression coefficient; B = Unstandardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B

7.6.4 Stress and pain: Mediation by psychosocial factors

The trauma diathesis stress model of widespread pain proposed a number of psychological and social variables as potential pathways through which stress might influence widespread pain. This section presents the results of the mediation analysis for adult attachment style, social support, health anxiety, somatosensory amplification and dissociation.

Figure 7.6 shows an example of the mediation models. The stress pain relationship was mediated by fearful attachment style and preoccupied attachment style, but not secure or dismissing attachment style, social support (see Table 7.18), health anxiety, somatosensory amplification or dissociation (Table 7.19).

Figure 7.6 Stress and pain mediated by fearful attachment style



Root mean square error of approximation (RMSEA) = 0.027
Standardised root mean square residual (SRMR) = 0.0541

PSe1-4 = error terms for anxiety, depression, somatic symptoms and threatening events; d1-2 = disturbance term for number of pain sites and fearful attachment style; LV = latent variable; numbers on arrows = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

Table 7.18 Psychological stress and number of pain sites at follow up mediated by adult attachment style and social support

Mediator			β	95% CI		P	B	R^2	a	b
Attachment Style	Secure	Indirect	-0.013	-0.034	0.002	0.094	-0.019	0.358	-0.298	0.044
		Direct	0.238	0.148	0.332	0.001	0.344		(-0.377, -0.218)	(-0.010, 0.102)
		Total	0.225	0.139	0.317	0.001	0.325			
	Dismissing	Indirect	0.001	-0.010	0.008	0.695	0.001	0.359	0.090	0.006
		Direct	0.228	0.141	0.323	0.001	0.332		(0.008, 0.175)	(-0.054, 0.064)
		Total	0.228	0.142	0.332	0.001	0.333			
	Fearful	Indirect	-0.030	-0.064	-0.001	**0.042***	-0.043	0.358	0.438	-0.069
		Direct	0.255	0.159	0.362	0.001	0.367		(0.362, 0.505)	(-0.139, -0.001)
		Total	0.225	0.138	0.316	0.001	0.324			
	Preoccupied	Indirect	-0.023	-0.050	-0.001	**0.041***	-0.34	0.360	0.335	-0.07
		Direct	0.253	0.158	0.349	0.001	0.365		(0.214, 0.419)	(-0.136, -0.001)
		Total	0.230	0.142	0.322	0.001	0.331			
Social Support		Indirect	0.002	-0.022	0.027	0.901	0.002	0.358	-0.297	-0.005
		Direct	0.222	0.134	0.319	0.001	0.326		(-0.402, -0.188)	(-0.084, 0.074)
		Total	0.223	0.140	0.316	0.001	0.328			

Analysis based on 737 participants; β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical value $p < 0.05$; ***Significant indirect effects in **red bold**

Table 7.19 Psychological stress and number of pain sites at follow up mediated by health anxiety, somatosensory amplification and dissociation

Mediator		β	95% CI		P	B	R^2	a	b
Health Anxiety	Indirect	0.002	-0.005	0.017	0.489	0.002	0.145	0.017 (-0.074, 0.116)	0.087 (0.000, 0.197)
	Direct	0.371	0.252	0.484	0.001	0.565			
	Total	0.373	0.257	0.483	0.001	0.567			
Somatosensory Amplification	Indirect	0.001	-0.004	0.014	0.412	0.002	0.140	0.024 (-0.083, 0.134)	0.055 (-0.030, 0.140)
	Direct	0.371	0.254	0.483	0.001	0.564			
	Total	0.373	0.257	0.484	0.001	0.566			
Dissociation	Indirect	0.000	-0.003	0.004	0.735	0.000	0.137	-0.003 (-0.083, 0.074)	-0.017 (-0.086, 0.065)
	Direct	0.372	0.257	0.484	0.001	0.565			
	Total	0.372	0.257	0.484	0.001	0.565			

Analysis based on 468 participants; β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical value $p < 0.05$; *Significant indirect effects in **red bold**

7.6.5 Stress and pain: Moderated mediation

Each of the mediation models examined in the previous section were next assessed to identify any moderation effects of childhood abuse and sex.

a) Moderation by childhood abuse

Attachment style mediated the stress pain relationship differently conditional on abuse status. For the fearful attachment style, the indirect effects were significant for the abuse group (β = -0.05, p = 0.003), but not for the no abuse (β = -0.03, p = 0.113) or frequent abuse groups (β = 0.03, p = 0.310) (Table 7.20). Similarly, for the preoccupied attachment style, the indirect effects were significant for the abuse group (β = -0.05, p = 0.008); however, when adjustments were made for multiple comparisons, this result was no longer significant (Table 7.21).

The stress pain relationship was not mediated by dismissing or secure attachment styles, social support, health anxiety, somatosensory amplification or dissociation, even when examining the no abuse, abuse and frequent abuse groups individually (Tables 7.22 and Appendix 4 Tables 6-10).

b) Moderation by childhood abuse and sex

When considering the three abuse groups (no abuse, abuse and frequent abuse) by sex, the stress pain relationship was not mediated by attachment style, social support, health anxiety, somatosensory amplification or dissociation after adjusting for multiple comparisons. The indirect effects for all three abuse groups failed to reach significance for both male and female participants (Tables 7.20-7.22 and Appendix 4 Tables 6-10).

Table 7.20 Psychological stress and number of pain sites at follow up mediated by fearful attachment style and moderated by childhood abuse and sex

			β	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.030	-0.077	0.008	0.113	-0.045	0.372	0.361	-0.083		
		Direct	0.315	0.174	0.467	<0.001	0.479		(0.243, 0.465)	(-0.191, 0.025)	RMSEA	0.026
		Total	0.285	0.153	0.427	<0.001	0.434				SRMR	0.0541
	Abuse	Indirect	-0.053	-0.132	-0.012	**0.003***	-0.083	0.336	0.331	-0.160		
		Direct	0.341	0.130	0.553	0.001	0.536		(0.128, 0.481)	(-0.295, -0.041)		
		Total	0.288	0.098	0.515	0.002	0.453					
	Frequent Abuse	Indirect	0.026	-0.026	0.086	0.310	0.039	0.408	0.457	0.057		
		Direct	0.075	-0.082	0.248	0.348	0.112		(0.324, 0.573)	(-0.059, 0.177)		
		Total	0.101	-0.041	0.253	0.161	0.151					
Males	No abuse	Indirect	-0.069	-0.165	0.016	0.098	-0.097	0.289	0.442	-0.155		
		Direct	0.427	0.170	0.651	0.004	0.600		(0.287, 0.580)	(-0.332, 0.042)		
		Total	0.359	0.128	0.578	0.006	0.504					
	Abuse	Indirect	-0.088	-0.284	-0.007	0.030	-0.139	0.357	0.451	-0.195		
		Direct	0.413	0.091	0.742	0.013	0.652		(0.190, 0.661)	(-0.447, -.012)		
		Total	0.325	0.048	0.659	0.021	0.513					
	Frequent Abuse	Indirect	-0.002	-0.079	0.061	0.950	-0.003	0.424	0.412	-0.005		
		Direct	0.173	-0.111	0.507	0.252	0.249		(0.189, 0.611)	(-0.169, 0.147)		
		Total	0.171	-0.077	0.481	0.182	0.246					
Females	No abuse	Indirect	-0.001	-0.046	0.033	0.949	-0.002	0.468	0.283	-0.003		
		Direct	0.229	0.083	0.393	0.002	0.370		(0.115, 0.454)	(-0.130, 0.113)		
		Total	0.228	0.094	0.384	0.001	0.368					
	Abuse	Indirect	-0.028	-0.121	0.003	0.103	-0.045	0.324	0.197	-0.141		
		Direct	0.241	-0.028	0.508	0.080	0.391		(-0.068, 0.405)	(-0.300, 0.030)		
		Total	0.214	-0.041	0.474	0.106	0.347					
	Frequent Abuse	Indirect	0.045	-0.031	0.157	0.252	0.073	0.399	0.469	0.096		
		Direct	0.015	-0.192	0.276	0.857	0.024		(0.272, 0.645)	(-0.082, 0.277)		
		Total	0.060	-0.128	0.281	0.528	0.097					

Analysis based on 737 participants: No abuse = 342, Abuse = 225, Frequent Abuse = 170. Males = 330: No abuse = 151, Abuse = 102, Frequent Abuse = 77. Females = 407: No abuse = 191, Abuse = 123, Frequent Abuse = 93. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006; ***Significant indirect effects in **red bold**

Table 7.21 Psychological stress and number of pain sites at follow up mediated by preoccupied attachment style and moderated by childhood abuse and sex

			B	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.019	-0.056	0.009	0.165	-0.029	0.371	0.272	-0.068		
		Direct	0.307	0.161	0.451	0.001	0.473		(0.152, 0.389)	(-0.173, 0.039)	RMSEA	0.027
		Total	0.289	0.148	0.425	0.001	0.445				SRMR	0.0526
	Abuse	Indirect	-0.047	-0.128	-0.009	0.008	-0.074	0.329	0.329	-0.144		
		Direct	0.332	0.110	0.541	0.002	0.517		(0.128, 0.511)	(-0.275, -0.029)		
		Total	0.285	0.077	0.499	0.006	0.443					
	Frequent Abuse	Indirect	-0.005	-0.061	0.043	0.784	-0.007	0.401	0.335	-0.014		
		Direct	0.113	-0.053	0.273	0.175	0.166		(0.147, 0.507)	(-0.153, 0.121)		
		Total	0.108	-0.034	0.259	0.143	0.159					
Males	No abuse	Indirect	-0.046	-0.121	-0.004	0.032	-0.066	0.287	0.301	-0.153		
		Direct	0.416	0.164	0.637	0.002	0.591		(0.130, 0.472)	(-0.290, 0.006)		
		Total	0.369	0.121	0.589	0.003	0.525					
	Abuse	Indirect	-0.047	-0.190	0.000	0.051	-0.074	0.346	0.312	-0.150		
		Direct	0.379	0.026	0.688	0.037	0.600		(0.014, 0.552)	(-0.362, 0.009)		
		Total	0.332	0.006	0.654	0.044	0.526					
	Frequent abuse	Indirect	-0.022	-0.057	0.003	0.083	-0.032	0.340	0.259	-0.086		
		Direct	0.328	0.170	0.483	0.001	0.476		(0.129, 0.382)	(-0.180, 0.017)		
		Total	0.305	0.154	0.463	<0.001	0.444					
Females	No abuse	Indirect	-0.002	-0.043	0.034	0.888	-0.003	0.469	0.248	-0.008		
		Direct	0.234	0.088	0.418	0.001	0.381		(0.077, 0.401)	(-0.142, 0.123)		
		Total	0.232	0.095	0.401	0.001	0.378					
	Abuse	Indirect	-0.041	-0.149	0.003	0.074	-0.063	0.315	0.330	-0.123		
		Direct	0.238	-0.072	0.508	0.129	0.370		(0.084, 0.557)	(-0.297, 0.034)		
		Total	0.197	-0.072	0.508	0.129	0.307					
	Frequent abuse	Indirect	-0.019	-0.062	0.018	0.287	-0.027	0.319	0.392	-0.048		
		Direct	0.177	0.056	0.290	0.004	0.257		(0.277, 0.503)	(-0.141, 0.051)		
		Total	0.159	0.057	0.263	0.003	0.230					

Analysis based on 737 participants: No abuse = 342, Abuse = 225, Frequent Abuse = 170. Males = 330: No abuse = 151, Abuse = 102, Frequent Abuse = 77. Females = 407: No abuse = 191, Abuse = 123, Frequent Abuse = 93. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006; *Significant indirect effects in **red bold**

Table 7.22 Psychological stress and number of pain sites at follow up mediated by dismissing attachment style and moderated by childhood abuse and sex

			β	β 95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	0.002	-0.005	0.016	0.453	0.002	0.368	0.084	0.019		
		Direct	0.287	0.154	0.433	<0.001	0.442		(-0.029, 0.198)	(-0.073, 0.106)	RMSEA	0.027
		Total	0.288	0.156	0.434	<0.001	0.445				SRMR	0.0507
	Abuse	Indirect	0.001	-0.006	0.016	0.562	0.001	0.335	-0.032	-0.020		
		Direct	0.316	0.129	0.536	0.001	0.531		(-0.188, 0.122)	(-0.122, 0.089)		
		Total	0.316	0.130	0.539	0.001	0.532					
	Frequent Abuse	Indirect	0.008	-0.010	0.048	0.254	0.011	0.406	0.146	0.053		
		Direct	0.095	-0.050	0.254	0.186	0.141		(-0.043, 0.340)	(-0.078, 0.163)		
		Total	0.102	-0.040	0.260	0.154	0.153					
Males	No abuse	Indirect	-0.004	-0.040	0.010	0.467	-0.005	0.263	0.113	-0.034		
		Direct	0.369	0.133	0.592	0.006	0.525		(-0.053, 0.263)	(-0.175, 0.102)		
		Total	0.365	0.135	0.589	0.005	0.519					
	Abuse	Indirect	-0.001	-0.039	0.009	0.534	-0.002	0.350	-0.071	0.018		
		Direct	0.349	0.081	0.658	0.008	0.569		(-0.314, 0.121)	(-0.116, 0.170)		
		Total	0.348	0.083	0.657	0.008	0.567					
	Frequent Abuse	Indirect	-0.007	-0.100	0.012	0.308	-0.010	0.430	0.088	-0.083		
		Direct	0.189	-0.049	0.492	0.114	0.271		(-0.193, 0.387)	(-0.280, 0.103)		
		Total	0.182	-0.062	0.481	0.136	0.260					
Females	No abuse	Indirect	0.004	-0.004	0.030	0.285	0.006	0.471	0.066	0.055		
		Direct	0.236	0.097	0.393	0.001	0.387		(-0.085, 0.217)	(-0.069, 0.166)		
		Total	0.239	0.100	0.398	0.001	0.393					
	Abuse	Indirect	0.000	-0.021	0.030	0.842	0.001	0.317	-0.007	-0.041		
		Direct	0.219	-0.040	0.493	0.096	0.377		(-0.246, 0.239)	(-0.204, 0.114)		
		Total	0.219	-0.040	0.484	0.101	0.377					
	Frequent Abuse	Indirect	0.047	0.003	0.140	0.032	0.080	0.445	0.239	0.196		
		Direct	-0.011	-0.192	0.212	0.938	-0.018		(-0.007, 0.457)	(0.048, 0.345)		
		Total	0.036	-0.147	0.252	0.692	0.062					

Analysis based on 737 participants: No abuse = 342, Abuse = 225, Frequent Abuse = 170. Males = 330: No abuse = 151, Abuse = 102, Frequent Abuse = 77. Females = 407: No abuse = 191, Abuse = 123, Frequent Abuse = 93. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006; *Significant indirect effects in **red bold**

7.7 Discussion

This section provides a summary of the findings from the GPSS study and a comparison to previous studies. The trauma diathesis stress model of widespread pain was assessed by progressively more complex models; the interpretation of the findings from each model are then discussed in turn. Following an examination of the strengths and limitations of the study, the implications of the findings for the trauma diathesis stress model of widespread pain are presented.

7.7.1 Summary of findings

The aim of the analysis presented in this chapter was to ascertain whether individuals with a history of childhood abuse had an increased susceptibility to widespread pain when they experienced psychological stress. To summarise, these results offer support for the trauma diathesis stress model of widespread pain proposed in Section 2.5 (pg50) and the hypotheses presented in Chapter 3.

(1) Among adults, an increase in psychological stress was associated with a higher number of pain sites in the cross-sectional analysis. Validation of the relationship in the prospective data confirmed this association.

(2) The relationship between psychological stress and number of pain sites was moderated by exposure to childhood abuse in the cross-sectional analysis. Specifically results show that the relationship between stress and pain was significantly stronger for

- Participants reporting any childhood emotional abuse compared to those reporting no childhood emotional abuse
- Participants reporting frequent abuse compared to those reporting no abuse.

The moderation of the stress pain relationship by childhood abuse was also moderated by sex, with the relationship being significantly stronger for

- Male participants reporting frequent abuse compared to male participants reporting no abuse, and

- Female participants reporting less frequent abuse compared to female participants reporting no abuse.

In the prospective analysis, however, the stress pain relationship was not moderated by childhood abuse or sex. Specifically, results show that

- There was no significant difference in the strength of the relationship between the three abuse groups: no abuse, abuse and frequent abuse
- The stress pain relationship was not significant for those reporting frequent abuse
- There was no significant difference in the strength of the relationship between the three abuse groups for males and females.

(3) The relationship between psychological stress and number of pain sites was mediated by adult attachment style. Specifically, results show that the stress pain relationship was mediated by

- Secure, fearful and preoccupied attachment style in the cross-sectional analysis, and
- Fearful and preoccupied attachment style in the prospective analysis
- The relationship was not mediated by social support, health anxiety, somatosensory amplification or dissociation.

(4) The mediation of the stress pain relationship by adult attachment style was moderated by childhood abuse and by sex in the cross-sectional analysis. Specifically, results show that the stress pain relationship was mediated by

- Secure attachment style for participants reporting frequent abuse
- Fearful attachment style for participants reporting abuse and frequent abuse
- Preoccupied attachment style for participants reporting abuse and frequent abuse.

This moderated mediation effect was also further moderated by sex. Specifically, results show that the stress pain relationship was mediated by

- Fearful attachment style for male participants reporting frequent abuse and female participants reporting no abuse, and
- Preoccupied attachment style for female participants reporting no abuse.

In the prospective analysis, fearful and preoccupied adult attachment style mediated the stress pain relationship and this mediation was also moderated by childhood abuse. Specifically, results show that the stress pain relationship was mediated by

- Fearful attachment style for participants reporting abuse
- The mediation by attachment style was not moderated by sex.

7.7.2 Comparison with previous studies

Whilst no studies have been identified which specifically report the number of sites of pain using the 29 site pain manikin, comparisons can be made with other studies using a pain site count. For example, using a count of ten pain sites, Hunt et al (1999) found that 43% of their community based population reported no pain, which is consistent with the findings of the current study (47.5% at baseline and 45.6% at follow up). Similarly, the persistence of widespread pain in the current study was consistent with previous research. For example, Kamaleri et al (2009) found that 46% of participants in their community based study reported pain in the same number of sites (plus or minus one), which was comparable to the rate of 50% in the current study. No significant difference was found in the number of pain sites reported by males and females, at either baseline or follow-up. Studies including Kamaleri et al (2008b) and Svebak et al (2006) have found a female predominance for musculoskeletal pain, whilst other prospective studies have not (e.g. Gupta et al, 2007, Jones et al, 2011). Previous research suggests that the prevalence of widespread pain increases until approximately 50 - 59 years of age for females and 60 – 69 years of age for males, and then begins to decline (see Table 1.1 pg7). The current study found a small but significant positive correlation between age and number of pain sites (baseline r=0.053; follow up r=0.083). On further examination this correlation was significant for females at baseline (r=0.085, p=0.015), but not for

males (r=0.009, p=0.832). This would suggest that the number of pain sites increases with age, particularly for females (median age 46 years).

The median scores for anxiety, depression and somatisation for the current study were consistent with previous research within general population samples, as described in section 5.4.4 (Crawford et al, 2001; Hammad et al, 2001). Similarly, the prevalence of childhood abuse and neglect in the GPSS population was broadly in line with previous studies detailed in Section 2.2.2a. The rates of 31%, 34%, 14% and 14% for physical, emotional, sexual abuse and neglect are consistent with rates obtained in previous population based studies of 29% (Haviland et al, 2010), 36% (Stoltenborgh et al, 2012), 13% (Stoltenborgh et al, 2011) and 16-18% (Stoltenborgh et al, 2013b) respectively. As shown by previous research, age, education, marital status, employment status, social support, attachment style, health anxiety, somatosensory amplification and dissociation were all associated with the number of pain sites in the bivariate analysis (as described in Section 2.5.2) (Bergman, 2005; Davies et al, 2009; Geisser et al, 2008; Leavitt & Katz, 2003).

The similarity of these findings with those of previous studies suggests that the results from the current study are independent of the study population and therefore would be generalisable to the general population.

7.7.3 Interpretation of SEM findings

a) Stress and pain

Confirmatory factor analysis was used to create a *psychological stress* latent variable by assessing the common variance amongst the observed variables for anxiety, depression, somatisation and recent threatening events. The *psychological stress* latent variable was a good representation of an underlying construct in the study population. No previous research has been identified which specifically combined these four factors into a latent variable. However, the relationship between anxiety, depression and

somatisation and the variance explained in each of these factors by the others was comparable with previous research. For example, Lowe et al (2008) found that 59% of the variance in depression was explained by anxiety and somatisation, 51% of the variance in anxiety was explained by depression and somatisation and 46% of the variance in somatisation was explained by anxiety and depression. This compared to 68%, 60% and 48% respectively in the current study, which also included recent life threatening events.

Using this latent variable, psychological stress was associated with the number of pain sites in both the cross-sectional (β = 0.51) and prospective analyses (β = 0.23). The SEM model was a good fit to the data and explained 26% (cross-sectionally) and 36% (prospectively) of the variance in the number of pain sites. Whilst the four factors of anxiety, depression, somatisation and life events have been consistently associated with widespread pain in cross-sectional and prospective analysis (for example Gupta et al, 2007; Holm et al, 2007; as detailed in Section 2.3.2), this was the first time the relationship had been assessed using all four factors combined in a latent variable. As described above, previous studies have also focused on reporting percentages and risks (odds ratios or relative risk), a comparison of effect sizes was therefore difficult. These results confirm the important role of psychological stress in the development and persistence of widespread pain.

b) Stress and pain: moderation by childhood abuse

(i) Individual childhood abuse types

As detailed in section 5.5a, the moderation effect on the stress pain relationship of each individual childhood abuse type was assessed in the cross-sectional analysis. Considered in this way, the only significant moderator was emotional abuse. The increase in psychological stress was associated with a significantly greater increase in the number of pain sites for those reporting childhood emotional abuse (β = 0.57) compared to those who did not (β = 0.45). Consistent with previous research (Smith et

al, 2010), childhood emotional abuse was the most common type of abuse, reported by 35% of the study population. Previous research has consistently failed to find any direct association between childhood emotional abuse and widespread pain (Hauser et al, 2011; Ruiz-Perez et al, 2009; Goldberg et al, 1999; Walker et al, 1997). The results from this current study therefore suggest an indirect pathway whereby childhood emotional abuse creates a susceptibility to widespread pain, as proposed by the trauma diathesis stress model of widespread pain.

(ii) Any childhood abuse or neglect

Whilst the above results focused on each individual type of abuse the literature shows considerable co-occurrence of abuse types (Edwards et al, 2003). This was also reflected in the results of this study. For example, of the 993 participants in the no physical abuse group (as shown in Table 7.6), 291 (29%) reported emotional abuse, sexual abuse and / or neglect. Of the no emotional abuse group, 243 (26%) reported one or more other types of childhood abuse. In order to account for this co-occurrence a variable "any childhood abuse or neglect" was created, as described in Section 5.5b) (pg 107). The moderation effect of this variable was then assessed in the cross-sectional analysis. Results show a non-significant trend (p=0.06) for the stress pain relationship to be stronger for those participants reporting any type of childhood abuse ($\beta = 0.52$) compared to those without an abuse history ($\beta = 0.45$).

(iii) Childhood abuse latent variable

The four individual childhood abuse type variables and the "any childhood abuse or neglect" variable were created by dichotomising the participants responses to the CSPAQ and PBI as described in Section 5.5 (pg107). Previous research suggests that multiple types of abuse and frequently occurring abuse lead to greater levels of traumatisation (Clemmons et al, 2007). In order to assess the impact of such a dose response of abuse on the stress pain relationship, a *childhood abuse* latent variable was created (see Section 5.5c, pg108). This latent variable fit the data well, suggesting that it

was a good representation of an underlying construct in the study population. Scores on this latent variable were used to create three participant groups: no abuse, abuse and frequent abuse. As hypothesised, cross-sectionally, the stress pain relationship was significantly stronger in those individuals reporting frequent abuse compared to those reporting no childhood abuse. When considered prospectively, however, there was no significant difference in the strength of the stress pain relationship between the three groups; in fact the trend for the moderation effect was not in the hypothesised direction. Baseline levels of psychological stress predicted the number of pain sites at follow up for individuals without an abuse history, but not for individuals reporting frequent abuse. So whilst the findings from the cross-sectional analyses are suggestive of the moderation effect of frequent childhood abuse, this was not confirmed in the prospective analysis. Possible explanations for the equivocal findings include potential recall bias and over-reporting, the strength of the confounding of baseline pain and the possibility that differing mechanisms are involved in the development and persistence of widespread pain. These potential explanations are discussed in turn.

Firstly, it is possible that the self-reports of individuals with widespread pain and / or high levels of psychological stress may be subject to recall bias including the mood congruent recall (Raphael & Cloite, 1994) and effort after meaning (Zaromb & Roediger, 2009) discussed in section 2.2.3c. Research suggests that individuals with widespread pain over-report other symptoms (Wolfe et al, 2012). The significant moderation effect found in the cross-sectional analysis may thus be an artefact of such over-reporting and bias. For example, those reporting more pain at baseline may have over reported the levels of psychological stress and / or childhood abuse they experienced. However, those participants reporting abuse at baseline still reported a significantly greater number of pain sites at follow up compared to individuals who reported no childhood abuse, suggesting little or no such over reporting. In order to obtain a clearer understanding of this potential reporting bias, it would be useful to obtain the same information at multiple time points (such as the reporting of childhood abuse and psychological stress at follow

up). Analysis could then be performed to assess whether childhood abuse was reported consistently over time, or whether it varied in relation to the reporting of pain.

Secondly, the main difference between the cross-sectional and prospective analysis was that in the prospective analysis the number of pain sites at baseline was statistically controlled for. Baseline pain was included in the prospective model as a confounder (as described in Section 4.6.6, pg90). The multiple group analysis assessed not only the stress pain relationship, but compared all the relationships within the model (see Figure 7.5) between the three abuse groups. The number of pain sites at baseline was a stronger confounder of the stress pain relationship for the frequent abuse group (β = 0.57) than the no abuse group (β = 0.42, p=0.07). This strong association between baseline and follow up pain thus reduced the predictive ability of stress for the frequently abused group. This suggests that the stress pain relationship may be different for individuals who have experienced frequent abuse in childhood. This analysis used the "controlling for baseline pain" model. Although this model was a better fit of the data than the "pain as a stressor" model (see Table 7.15), the latter did still meet the model fit criteria specified in Section 4.6 (SRMR ≤0.09 and RMSEA ≤0.06). It may be that the experience of pain becomes more of a stressor for individuals who have experienced frequent abuse. It would therefore be interesting to examine these relationships using the "pain as a stressor" model to discover whether this would produce consistent results for both the cross-sectional and prospective analysis.

Finally, this difference in the stress pain relationship between the abuse groups may also indicate that different mechanisms are involved in the development and maintenance of widespread pain. For example, in a study examining the association between back pain and lifetime abuse, abuse was shown to increase the risk of the development of back pain (OR 2.65) over the 12 month period of the study. However, abuse was not associated with an increase in pain in those already with pain at baseline (Linton, 2002). Although Linton's study explored a direct association between lifetime

abuse and back pain, rather than the moderation of the stress pain relationship examined in this current study, the similarity of findings suggest that the development and the persistence of painful conditions may involve different processes. Childhood abuse may factor only in the development of widespread pain, but once it has developed, abuse status may have no further influence on the number of sites of pain. In order to examine this further, it would be necessary to assess the moderation effect of childhood abuse in those individuals without pain at baseline, but with pain at follow up. Unfortunately, only 116 participants met this criteria in the current study, a sample too small for meaningful moderation analysis within SEM.

As described in Section 2.2.2 (Table 2.1, pg26), the results from previous research exploring a direct association between childhood abuse and widespread pain was inconclusive, with ten studies finding an association and five finding no association. By examining the relationship in a different way, with psychological stress as the predictor and trauma as the moderator, the relationship between these factors has been clarified. These findings also support those of Raphael et al (2011). Childhood abuse alone seems to be insufficient to lead to the development of widespread pain; but child abuse does increase an individual's susceptibility to the subsequent development of widespread pain when they become stressed.

c) Stress and pain: moderation by childhood abuse and sex

In the cross-sectional analysis, the stress pain relationship was moderated by childhood abuse differently for males and females. Compared to individuals without an abuse history, the stress pain relationship was significantly stronger for males reporting frequent abuse and for females reporting abuse. For male participants, the experience of less frequent abuse seemed to offer some protection against the damaging effects of psychological stress. This finding appears consistent with research examining the long term effects of adversity, whereby combat exposure and non-abusive life events have been found to have a U shaped relationship with negative outcomes. Individuals who

report moderate levels of prior adversity are less negatively affected by more recent negative events than individuals with no or high levels of prior adversity (Schnurr, et al, 1993; Seery et al, 2010a; 2010b; Clements & Turpin, 2000). For males, it is therefore possible that less frequent childhood abuse produced a "stress inoculation" (Seery, 2011, pg390) effect, reducing the impact of subsequent stressors, whilst frequent abuse increased the effects. The stress pain relationship in female participants in the current study was significantly stronger in the abuse group compared to the no abuse group. The potential protection afforded to male abuse participants was not found for females. As with the moderation by childhood abuse, these sex differences were not confirmed in the prospective analysis.

How does childhood abuse increase an individual's susceptibility to widespread pain when they experience psychological stress? Childhood abuse can have short and long term biological, psychological and social implications. Biologically, childhood abuse can result in disruptions to the nervous, endocrine and immune systems (Kiecolt-Glaser et al, 2011; Dube et al, 2009; Heim et al, 2009). For example, childhood abuse has been associated with increased basal cortisol levels, changes in diurnal cortisol rhythms (Chugani et al, 2001) and a blunted ACTH response to stress in childhood (Tarullo & Gunnar, 2006). There may be "sensitive periods" in a child's development during which childhood abuse and neglect can be particularly damaging. A study examining the long term effects of evacuation, and thus separation from both parents during World War Two, showed a heightened stress response only in participants evacuated between the ages of 2 and 7 years; not in younger or older children (Pesonen et al, 2010). Although this research did not take into account subsequent life experiences, it suggests that the "sensitive period" occurs earlier than the age limit set for childhood abuse in the current study: prior to age 16 years. In support of this, other studies have found significant effects when examining childhood abuse occurring at a younger age. For example, Castro et al (2005) found significant direct associations between FM and self-reported childhood abuse occurring before age eleven, but not abuse occurring between ages 12

and 15 years. Similarly, Raphael and Widom (2011) found that court-documented childhood abuse occurring before age 11 moderated the relationship between PTSD and the extent and inference of pain. Furthermore, developmental research suggests that the frontal cortex, associated with both stress (Diorio et al, 1993) and pain (Derbyshire et al, 2000) continues to develop during adolescence (age 8 to 14 years) (Lupien et al, 2009) and that the full maturation of the HPA axis function occurs around puberty (Tarullo & Gunnar, 2006).

In adults who experienced abuse as children, alterations manifest as decreased cortisol (Carpenter et al, 2011) and increased ACTH responses to stress (Heim et al, 2000), and increased levels of pro-inflammatory cytokines and shorter telomeres, indicating greater cell aging (Kiecolt-Glaser et al, 2011). These changes potentially alter the thresholds and sensitivity of the stress and pain processing system (Heim et al, 2010; Glaser et al, 2006; Sansone et al, 2009; Jovanovic et al, 2009). These physiological factors were not assessed in this study; however, a number of potential psychological and social mediators were considered.

d) Stress and pain: mediation by psychosocial factors

As hypothesised, adult attachment style significantly mediated the stress pain relationship both cross-sectionally and prospectively, although the effect was small. Secure (having a positive view of the self and others), fearful (a negative view of the self and others) and preoccupied (negative view of the self and a positive view of others) attachment styles mediated the relationship cross-sectionally. The findings for fearful and preoccupied attachment styles were confirmed in the prospective analysis.

Social support, health anxiety, somatosensory amplification and dissociation were all significantly associated with the number of pain sites at both baseline and follow up. However, these factors did not mediate the stress pain relationship. This may be because there was no mediation effect to find, or because of problems with the

measurement or analysis of this information. In order to assess for mediation in SEM, the predictor, mediator and outcome variables should show some correlation; however, if the predictor and mediator variables are measured at the same time this may lead to an over-estimation of this relationship (the a path) and an under-estimation of the relationship between the mediator and the outcome (the b path). In the cross-sectional analysis all variables were measured at same time and in the prospective analysis, only the outcome variable was measured independently. So the lack of mediation by social support, health anxiety, somatosensory amplification and dissociation could be an artefact of the timing of these measurements (Preacher & Hayes, 2008).

The lack of significant mediation effects may also be due to the way the factors were measured or analysed. With regard to social support, this was measured using a dichotomous variable, which is not ideal for mediation analysis (Warner, 2013), and also over-simplifies a complex concept. For example, individuals vary in the amount of social support they require and social ties and contacts vary in their value and benefit to the individual (Abbott, 2009). So this imprecise measurement may explain the lack of mediation found. Theoretically, the concepts of health anxiety and somatosensory amplification are closely related, as evidenced by the strong correlations (Tables 7.2 and 7.4). So whilst no mediation effect was found for these concepts when examined individually, it would be interesting to examine these factors together, either as a latent variable or consecutively in a causal chain, such that psychological stress leads to health anxiety, which leads to somatosensory amplification, which results in widespread pain.

e) Stress and pain: moderated mediation

The moderated mediation analysis was performed in order to identify whether the mechanisms by which stress leads to widespread pain differ between individuals who reported childhood abuse and those who did not. The mediation of the stress pain relationship by adult attachment style was conditional on childhood abuse in the cross-sectional analysis. Secure, fearful and preoccupied attachment styles significantly

mediated the stress pain relationship, but only for individuals experiencing childhood abuse. This effect for fearful attachment style was also confirmed in the prospective analysis.

(i) Mediation by attachment style moderated by childhood abuse

Maunder and Hunter (2001) have proposed three pathways via which attachment styles may influence physical health: via alterations to the stress processing system, by the use of external regulators of affect, and by a reduced use of protective factors. Path one involves the perception of, and response to, stress. As mentioned above, the stress response system continues developing until around the time of puberty. The initial functioning of the stress response system and its subsequent development are highly dependent upon the responses of the caregivers. The "growth-facilitating emotional environment" (Schore, 2002, pg15) of a secure attachment enables the child to develop appropriate emotional responses and coping strategies leading to self-regulation. An insecure attachment, however, can result in impaired affect regulation. In support of this, preoccupied and fearful attachment styles have been associated with an increased perception of stress (Maunder et al, 2006; Kidd et al, 2011). Fearful attachment style has also been associated with increased stress reactivity (Powers et al, 2006) and slower recovery from stressful events (Halpern et al, 2011). The higher stress reactively associated with both fearful and preoccupied attachment styles could potentially exacerbate the disruption caused to the stress, immune and pain processing systems by the prior experience of trauma (as described in Section 2.5.2).

The second pathway by which attachment style influences health involves the use of external affect regulators. Due to their impaired internal affect regulation, individuals with insecure attachments may use behavioural strategies "to soothe, to distract, or to excite" (Maunder & Hunter, 2001, pg562). These strategies include increased smoking and alcohol use, low levels of physical exercise, poor diet and drug dependence (Huntsinger & Lueken et al, 2004; Maunder & Hunter, 2001), which have also been

associated with the development of widespread pain (VanDenKerkhof et al, 2011; Glass et al, 2004; Zvolensky et al, 2010).

The third pathway involves the reduced use of protective factors such as seeking treatment and social support. Individuals with fearful and preoccupied attachment styles experience more symptoms than those with secure and dismissing attachment styles, (Waldinger et al, 2006; Ciechanowski et al, 2002); however, fearful and preoccupied individuals differ in their health care seeking behaviour. Individuals with fearful attachments have the lowest primary care visits and costs, whilst preoccupied individuals have the highest (Ciechanowski et al, 2002). Preoccupied individuals have a positive view of others and therefore are more likely to seek treatment and social support (Ciechanowski et al, 2002; Ognibene & Collins, 1998). On the other hand, due to their belief that they are unworthy of care and their distrust of others, fearfully attached individuals are less likely to seek treatment or social support in times of stress (Ognibene & Collins, 1998). This delay in treatment seeking is likely to exacerbate symptoms, increasing the risk of the development and persistence of physical health problems (Maunder & Hunter, 2001).

The experience of childhood abuse has been consistently associated with insecure attachment styles in childhood (Baer & Martinez, 2006). By detrimentally affecting the stress system, affect regulation and behaviour, childhood abuse can change a child's normal developmental trajectory (Schore, 2002). Although attachment styles are moderately stable throughout life (Bowlby, 1969), they are flexible to change as new information is obtained from new experiences (Kirkpatrick & Davies, 1994; Davila et al, 1997; Cozzarelli et al, 2003). The formation of successful close personal relationships in adulthood can change an individual's attachment style and again change life's trajectory (Thomas & Hall, 2008). In some individuals, the biological, psychological or social alterations caused by childhood abuse can be reduced or reversed by the formation of a secure attachment in adulthood (Valentine & Feinauer, 1993; Runtz &

Schallow, 1997). The mediation effects of adult attachment style in the current study were significant but small. It is possible that adult attachment style may be a reflection of an individual's resiliency (Glaser, 2000), in which case attachment style may act as a moderator of the stress pain relationship, as proposed by Meredith et al (2008). It would be interesting to assess this possibility in future studies.

(ii) Mediation by attachment style moderated by childhood abuse and sex

When examining the moderation effect of sex, different patterns of moderated mediation were found. The results suggest that for frequently abused males, fearful attachment style provides a partial explanation of how stress leads to widespread pain. However, fearful and preoccupied attachment styles partially explained the stress pain relationship only for females without a history of abuse. Although this sex difference was not confirmed in the prospective analysis, these results could suggest that stress leads to widespread pain via different pathways in males and females dependent upon their early childhood experiences.

Explanations for the sex differences include the types of childhood abuse experienced, the response to trauma and developmental differences. In the current study, males were more likely to report physical and emotional abuse than females, whilst females reported more sexual abuse and neglect than males. Different types or combinations of types of abuse may have differing long term psychological and physical consequences (Trickett & McBride-Chang, 1995). For example, physical abuse has been associated with criminal and anti-social behaviour, sexual abuse with re-victimisation and neglect with social withdrawal (Finzi et al, 2000). However, there are considerable similarities and overlaps in the adverse outcomes associated with each abuse type (Mullen et al, 1996). This is likely due to the fact that abuse types often co-occur as in the current study; 55% of those reporting abuse reported multiple types of abuse. With regard to the response to trauma, compared to males, females tend to respond with greater negative affect, lower physiological arousal (Ordaz & Luna, 2012),

and have a reduced likelihood of resilience following trauma (Bonanno et al, 2007). For example, following a traumatic explosion, females experienced significantly higher levels of anxiety, depression, negative affectivity, dissociation and PTSD than males. PTSD severity and symptoms were predicted by depression and dissociation in females, but by anxiety in males, suggesting that males and females respond differently to trauma and that different pathways lead to PTSD (Christiansen & Elklit, 2008).

Research also suggests that central and autonomous nervous systems develop at differing rates for males and females (Schore, 2002), which may result in differing sensitive periods for deleterious effects. The association between adult attachment style and the physiological response to stress has also been found to differ between males and females (Powers et al, 2006). Why fearful attachment style mediates the stress pain relationship for frequently abused males, but fearful and preoccupied attachment styles mediate the relationship for non-abused females deserves further consideration. Future research could examine whether the moderation effect of different combinations of types of abuse are mediated by different attachment styles and further moderated by sex. However, this would require a large sample to cater for the number of combinations of abuse types.

(iii) Mediation by social support, health anxiety, somatosensory amplification and dissociation moderated by childhood abuse

It was anticipated that social support, health anxiety, somatosensory amplification and dissociation would mediate the stress pain relationship differently dependent upon abuse status. However, this was not the case.

Previous research was highly suggestive of the role of dissociation in the development of widespread pain in individuals who have experienced childhood abuse (Fillingim & Edwards, 2005). For example, compared to individuals without an abuse history, individuals who report childhood abuse demonstrate decreased pain sensitivity

(Fillingim & Edwards, 2005) but higher pain intensity ratings (Granot et al, 2011) in experimental pain studies. This complex pattern of changes affecting both sensory and affective components of pain perception has led some researchers to consider the role of dissociation as a mechanism by which trauma leads to pain (Fillingim & Edwards, 2005). However, dissociation was not a significant mediator of the stress pain relationship for individuals with or without an abuse history. As with the other psychosocial mediators discussed above, the finding of no mediating effect in the current study may be related to the timing of the assessment of dissociation, the method of assessment or the nature of the interaction of factors. Dissociation is an unconscious process which is difficult to assess using self-report measures (Cramer, 2000) and thus may be better assessed by a clinically trained interviewer (van Der Kolk et al, 2007a). Although the DES-T has been assessed as valid and reliable (see Section 5.5.4), its use has not been without issue (Giesbrecht et al 2007; Watson, 2003; Leavitt, 1999). Dissociation may be reflective of the severity of the impact of childhood abuse and as such may alter an individual's susceptibility. As such, dissociation may act as a moderator of the relationship rather than a mediator (McFarlane & Yehuda, 2007).

To summarise, the cross-sectional analysis indicates that childhood abuse and sex moderate the stress pain relationship. This suggests that the experience of any abuse in childhood for females, and frequent abuse for males, created or increased susceptibility. This susceptibility then increased the risk that subsequent psychological stress would lead to the development of widespread pain. The relationship between stress and pain was mediated by adult attachment style differently for males and females conditional upon their abuse status. An insecure adult attachment style may have detrimentally altered the stress and pain processing systems and the use of external effect regulators and protective factors, leading to the development of widespread pain in males who had experienced frequent abuse and females who had not experienced childhood abuse.

7.7.4 Strengths of the study

This study differed from previous research regarding trauma, stress and pain in its design and sampling frame, and its assessment of pain, psychological stress and childhood abuse. These factors are discussed in turn.

a) Study design

As detailed in Section 2.2.2c, the majority of previous childhood abuse and pain research has focused on exploring a direct association between widespread pain and individual types of childhood abuse, without assessing the severity of abuse. Few studies have considered the role of psychological stress or used multivariable analysis and the populations studied have tended to be female patients. The current study extends previous research by considering the association between psychological stress and widespread pain and the moderation effect of childhood abuse in both males and females in a population sample using novel analysis techniques.

Despite the evidence to suggest that the causes of widespread pain are multifactorial, previous studies examining the relationship between childhood abuse and pain have rarely considered any mediator or moderator analysis or employed testable theoretical models. This current study involved the testing of a diathesis stress model based on current theoretical understanding of pain, stress and trauma and on empirical evidence. The use of structural equation modelling also allowed for the simultaneous assessment of multiple factors. In addition to the moderation analysis, mediation by psychological and social factors and moderated mediation analysis have enabled an assessment of the pathway from psychological stress to widespread pain.

b) Sampling frame

Previous studies have focused mainly on the association between childhood abuse and pain in patient samples. Research suggests that patients with widespread pain may be different to community members with widespread pain with regard to pain intensity,

negative affect, fatigue and daily functioning (Kersh et al, 2001). This study used a community sample, obtained using general practice registers. The advantage of this sampling technique is that approximately 98% of people in the UK are registered with a GP (Lis & Mann, 1995) regardless of health status, age or ethnicity (Lewis et al, 2009). The sample was therefore highly likely to be representative of the general UK population and thus the results of the study generalisable. Details are also available to enable the analysis of non-participation bias, for example, age and gender.

c) Number of pain sites

The use of a simple count of the number of pain sites has a number of advantages over the use of clinical diagnostic criteria. As described in Section 1.3.3, levels of pain fluctuate over time. The use of a dichotomised measure can lead to the loss of important information with regard to individual differences between group members, a loss of power and effect size, and may result in a failure to recognise non-linear relationships (MacCallum et al, 2002). Using the ACR or other diagnostic criteria could therefore result in a misclassification of participants, whereas a count of the number of pain sites gives a more accurate representation, being less influenced by these fluctuations. The count of the number of pain sites provides a finer level of detail and better reflects the experience of pain: “The question is not ‘‘have you got it”? but ‘‘how much of it have you got”?” (Croft, 2009, pg6). The number of pain sites offers a simple measure which allows for the assessment of risk, is strongly associated with physical and psychological functioning and is more reflective of the experience of widespread pain than a dichotomised measure. A count of the number of pain sites thus potentially offers the optimum method for assessing the aetiology of widespread pain.

d) Psychological stress

Rather than assessing the relationship between pain and the individual factors of anxiety, depression, somatisation and life events, this study combined the effects of these factors in a latent variable. Research suggests that although each of these factors

produce a unique pattern of impairment, they are highly co-morbid and are more strongly associated with functional impairment when combined than individually (Lowe et al, 2008). Indeed in this current study, correlation results and model fit indices indicate this was the case.

e) Frequency of childhood abuse

Even though research shows that individuals frequently report multiple types of abuse and that detrimental impact has a dose response, the majority of previous studies have assessed the impact of each abuse type individually, most often in a dichotomised analysis without consideration of abuse frequency. The current study addressed this issue by firstly examining the unique influence of each individual type of childhood abuse and secondly using a latent variable to assess the impact of multiple types of abuse and the frequency of the occurrence of abusive experiences.

7.7.5 Limitations of the study

A number of limitations with the current study have been identified. These include the size of the sample and the assessment of widespread pain and childhood abuse. These factors are discussed in turn.

a) Sample size

One possible explanation for the difference between the cross-sectional and prospective findings is that the follow up sample size was insufficient to correctly estimate the parameters. This would increase the standard errors around estimates, reduce study power and increase the risk of a type II error (failing to reject the null hypothesis when it is false) (Park, 2004). For SEM, the sample size depends upon the distributional characteristics of the observed variables, the model complexity and the estimation method used (Lei & Wu, 2007). The recommended number of participants required varies considerably, with some researchers suggesting between 10 and 20 participants per variable (Schumaker & Lomax, 2004) and others recommending

between 100 and 200 participants for sufficient power in mediation analysis (Preacher & Hayes, 2007). In the prospective moderation analysis, the frequent abuse group size was reduced to below 100 participants for both males (77) and females (93) and may thus have been insufficient to correctly identify moderation and mediation effects.

b) The assessment of widespread pain

The use of the number of pain sites as an outcome measure has its limitations. It is still possible that a number of participants experienced pain, but not at the time of the two surveys. Although the questionnaire asked about pain lasting greater than one day in the last month, some participants may have experienced pain in the months prior to the baseline and / or follow up study, but not within a month of their completion of the survey. Further, this study only examined the number of sites of pain and did not include any measures related to the severity or impact of pain. Although research shows a clear linear relationship between number of pain sites and physical and psychological functioning (Kamaleri et al, 2008a; Section 1.3.3), a more clearly defined phenotype would include the severity of pain and its impact on physical functioning. This would enable an ascertainment of whether childhood abuse and neglect moderate the impact of pain as well as its widespreadness.

c) The assessment of childhood abuse

Issues relating to the assessment of childhood abuse in the current study include the use of self-report measures and the definitions of childhood abuse.

Self-report and recall bias

With regard to the use of self-report measures, reporting of childhood abuse can be affected not only by the pain specific bias discussed above (over-reporting), but also due to forgetting or embarrassment (under-reporting) (Gilbert et al, 2009). For example, in a prospective cohort study examining the difference in pain symptoms between participants with court documented abuse and age, sex, race and social class matched

participants, Raphael et al (2001) found that 73% of their participants with documented cases of abuse failed to self-report childhood abuse, whilst 49% of participants without documented cases self-reported some form of childhood abuse. Further research has replicated these findings, concluding that false positive was less likely than false negative recall (Hardt & Rutter, 2004; Putnam, 2003). If participants in the current study under reported childhood abuse or reported less frequent abuse than they actually experienced, then this would result in an underestimation of the moderating effects of childhood abuse. Alternative methods of assessing childhood abuse include interviews and documented cases. Research suggests that interviews have no clear advantage over questionnaires (Mullen et al, 1993), as face to face interviews may lead to social desirability responding (Podsakoff et al, 2003) and although they are perceived to allow for more detailed questioning and clarification, it could be argued that questionnaires provide privacy and anonymity that may be more conducive to the disclosure of such sensitive information (Hardt & Rutter, 2004). With regard to documented abuse, official confirmation of abuse is difficult as few cases are bought to the attention of the authorities. Prospective studies, following children with a court documented abuse history, may also be measuring different processes, as the subsequent experience of such child abuse may be very different to that of an unidentified abuse victim (Kendall-Tackett et al, 2004). The identified child faces a different set of challenges. For example, some may be supported and offered counselling / therapy (Jonzon & Lindblad, 2005; Van Houdenhove & Egle, 2002), whilst others may be ostracised and isolated (Alaggia, 2010). There may also be the potential for additional trauma, in the form of court cases, family disruption and relocation, especially if the perpetrator was a family member (Smith et al, 2000). Retrospective self-report and documented prospective studies provide complementary information regarding the long term consequences of childhood abuse (Shaffer et al, 2008).

Definitions of childhood abuse

As well as the self-report nature of the childhood abuse measure, the definitions used

for childhood abuse must also be considered. Some childhood sexual abuse measures exclude non-contact activities (Anda et al, 2006; Finestone et al, 2000) or treat them as a separate category such as sexual harassment (Van Houdenhove et al, 2001). Other measures stipulate the use of force or threat (e.g. Leserman et al, 1996) even though force may not be necessary if an individual is too young to understand the situation. Similarly, some measures require a child to have physical injury in order for a classification of physical abuse to apply (Goldberg et al, 1999). It could be argued that the effects of childhood abuse in the current study have been reduced by the inclusion of non-contact, non-threatening sexual abuse and non-injurious physical abuse, however, other research suggests that these experiences can be as distressing as those including contact, force and causing injury (Hart-Johnson & Green, 2012).

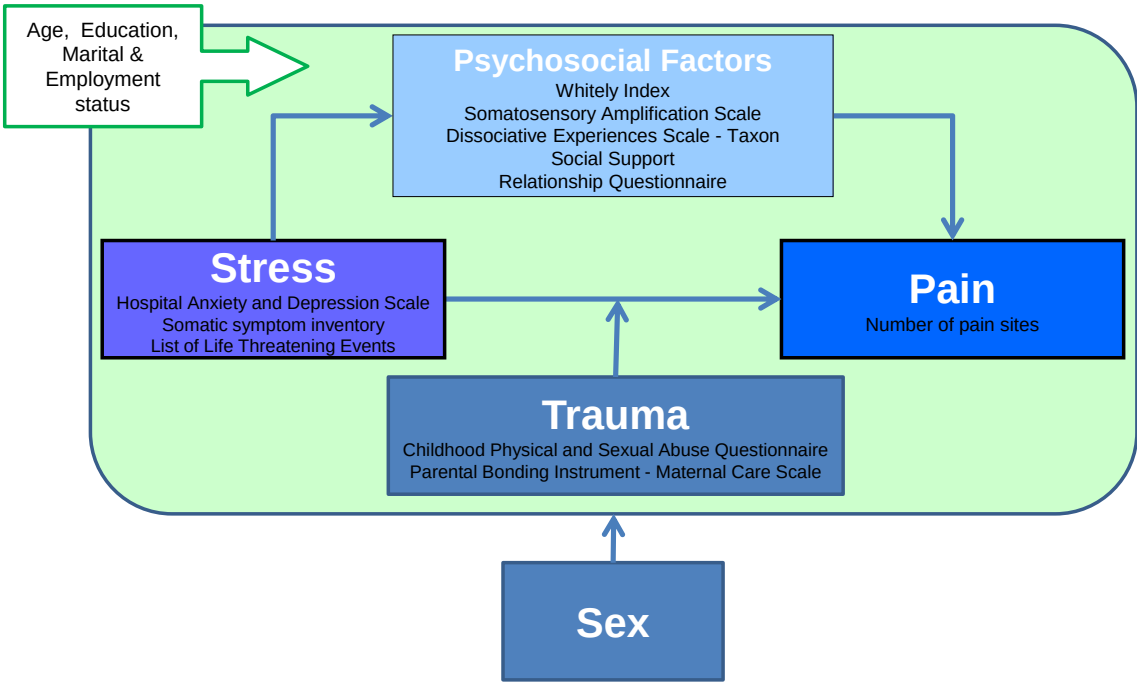
There is also a debate as to whether childhood sexual abuse is actually traumatic or not. For example, in a study by Geraerts (2006) 85% of sexual abuse victims "failed to appreciate their abuse as traumatic at the time it occurred" (Clancy, 2009, pg59). The participants reported that their abuse took place in a loving and / or playful context, which left them confused. They did not understand what it was that was happening. However, it is possible that the later realisation was traumatising; leading to shock and feelings of betrayal, powerlessness, stigmatisation, guilt and shame; factors associated with causing traumatic reactions (Finkelhor & Brown, 1985; Freyd et al, 2005). It may not necessarily be childhood abuse *per se* but an individual's reaction to abuse that leads to physical health problems, whether these reactions occur immediately during the abuse or some time later (Schnurr & Green, 2004a).

7.7.6 Key findings and implications for the trauma diathesis stress model of widespread pain

This section revisits the trauma diathesis stress model of widespread pain presented in Sections 2.5 (pg50) and 5.5 (pg106). Following a summary of the contribution made

to the field, a refined trauma diathesis stress model is presented, reflecting the key findings from the current study.

Figure 7.7 Proposed childhood abuse diathesis stress model of widespread pain



Source: original

a) Contribution to the field

This research has contributed to new knowledge firstly by testing a theoretical model, developed by the author (Figure 7.7). This model conceptualised the relationship between trauma, stress and pain in a novel way, within a diathesis stress framework. Using sophisticated statistical techniques to test the trauma diathesis stress model of widespread pain enabled an examination of the relationship between psychological stress and widespread pain, the identification of individuals who were susceptible to widespread pain when stressed (moderators) and also the pathways (mediators) by which psychological stress leads to widespread pain.

b) Key findings

1) Childhood abuse moderates the stress pain relationship

The relationship between psychological stress and widespread pain was well

established (Gupta et al, 2007; McBeth et al, 2007). However, not everyone who experiences psychological stress develops widespread pain. This current research has contributed to the knowledge base by identifying childhood abuse and sex as susceptibility factors. As discussed in Section 2.2.2b (pg26), previous research assessing a direct association between childhood abuse and widespread pain has been inconsistent. It was hypothesised that examining the relationship between childhood abuse and pain in a different way, using a diathesis stress framework, would provide more clarity. The results of the cross-sectional analysis suggest that childhood abuse and neglect created a susceptibility, increasing the risk that subsequent psychological stress leads to widespread pain. However, the different findings from the cross-sectional and prospective analysis warrant further investigation. There are many factors associated with the experience and subsequent impact of childhood abuse and neglect. Such factors include age and / or development stage at which abuse occurs (Glaser, 2000), the definition of abuse used, the relationship to the perpetrator (Finkelhor & Browne, 1985), the timing and response to any disclosure of abuse (O'Leary et al, 2010), the frequency and severity of experiences (Ruiz-Perez et al, 2009), the child's temperament (Schore, 2002) and the presence of a secure attachment in childhood (Styron & Janoff-Bulman, 1997). Future research should seek to clarify which of these factors are also relevant to the development of a susceptibility to widespread pain.

2) Adult attachment style mediates the stress pain relationship

The identification of the mediating effect of adult attachment style was also a major contribution of this study. In the cross-sectional analysis, the stress pain relationship was mediated by secure, fearful and preoccupied attachment style, but only for individuals experiencing childhood abuse. This effect for fearful attachment style was confirmed in the prospective analysis. Previous research has shown associations between adult attachment style and widespread pain (Davies et al, 2009), psychological stress (Waldinger et al, 2006) and childhood abuse (Aspelmeier et al, 2007). However,

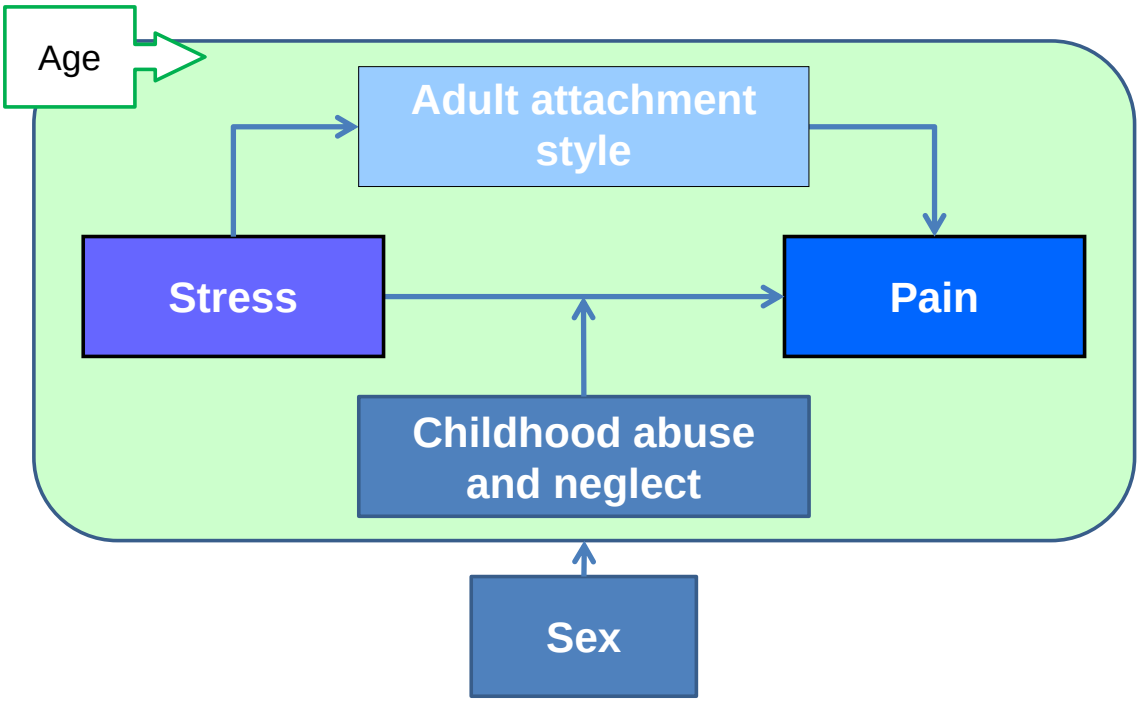
the results of the current research provided evidence of the mediation effect of attachment style, clarifying one of the mechanisms by which psychological stress leads to widespread pain.

3) The relationships are different in males and females

This current research also extends previous knowledge with regard to the sex differences found in both the moderation and mediation analyses. Compared to the no abuse groups, the stress pain relationship was stronger for the frequent abuse group for males and the abuse group for females. It was shown that childhood abuse increased susceptibility to the development of widespread pain, but the severity of the abuse required to increase susceptibility varied between males and females. The mediation of the stress pain relationship by attachment style was also conditional upon abuse status and sex. Fearful attachment style mediated the stress pain relationship for males who had experienced frequent abuse, whilst fearful and preoccupied styles mediated the relationship for females without an abuse history. This seems to suggest that stress leads to pain via different pathways for males and females.

In light of the findings from the current study, the trauma diathesis stress model of widespread pain has been refined (Figure 7.8). The adapted model shows a direct association between stress and pain, mediated by adult attachment style and moderated by childhood abuse and neglect and by sex.

Figure 7.8 Adapted childhood abuse diathesis stress model of widespread pain



Source: original

7.8 Chapter summary

This chapter presented the results of the analysis of the trauma diathesis stress model of widespread pain. Cross-sectionally, an increase in psychological stress was associated with a higher number of pain sites. This stress pain relationship was moderated by childhood abuse and sex and was mediated by adult attachment style. This mediation effect was also moderated by childhood abuse and sex. Prospectively, psychological stress was found to predict pain, except for those participants reporting frequent abuse. As with the cross-sectional analysis, the stress pain relationship was mediated by adult attachment style. The aim of this study was to identify whether childhood abuse and neglect increased susceptibility to widespread pain in individuals who experience psychological stress, and this was supported in the cross-sectional analysis. Potential explanations for the findings were discussed along with an examination of the strengths and limitations of the research, the implications of the findings for the trauma diathesis stress model and the contribution this study has made to the trauma, stress and pain field. The implications of the findings for the treatment of widespread pain and the recommendations for future research are described in Chapter 11.

To summarise, the key findings from the GPSS analysis are that the stress pain relationship was moderated by childhood abuse and mediated by adult attachment style. These relationships were also found to be different in males and females.

Chapter 8 North Staffordshire Osteoarthritis Project: Method

8.1 Chapter overview

The moderation effect of physically traumatic events on the relationship between psychological stress and widespread pain was assessed prospectively using data from the North Staffordshire Osteoarthritis Project (NorStOP). This chapter describes the methodology of the NorStOP study, including study design, procedure, sampling frame and the study questionnaire. As with the GPSS study, the design or development of the questionnaire, and the initial data collection activity was completed prior to my involvement with the study. I was, however, responsible for the data collection activity relating to adult physical trauma. Firstly I established which of the GP read codes related to physically traumatic experiences and secondly I identified which of the participants had those read codes recorded on their medical records (as described in Section 5.4.3). I also determined which of the previously collected data items were relevant to my study (as detailed in Section 8.4) and how those data items would be used to test the trauma diathesis stress model of widespread pain (as described in Section 8.5).

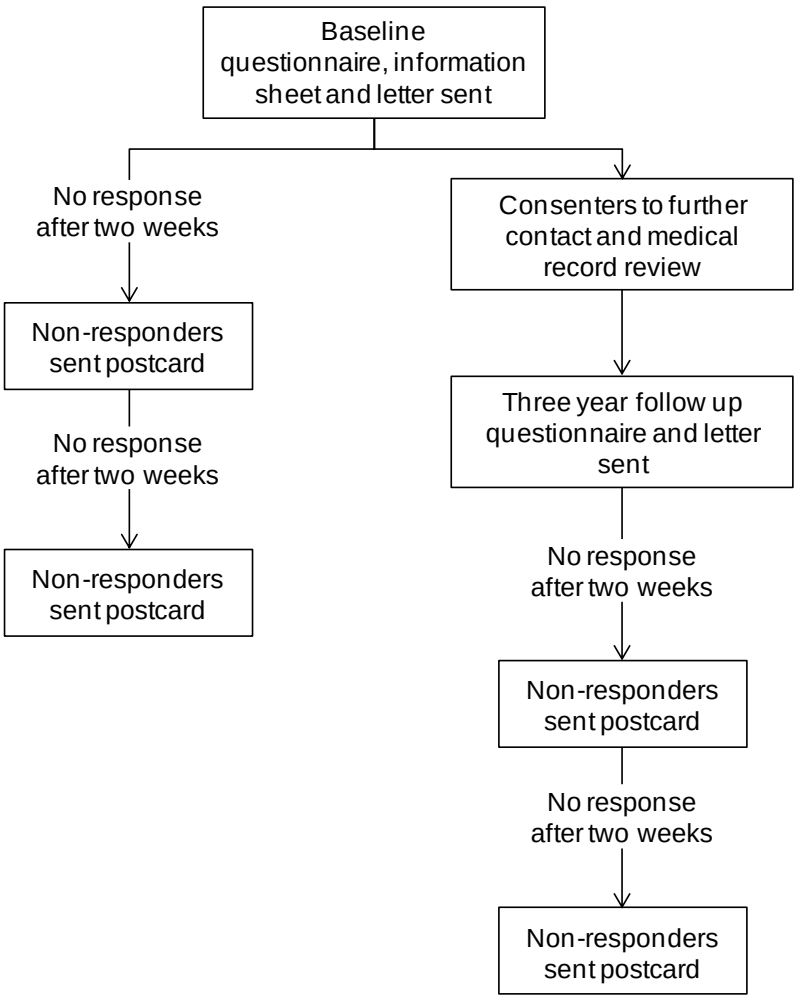
8.2 NorStOP study design and procedure

The NorStOP study was a population based longitudinal postal survey. This epidemiological study was designed to describe the prevalence of pain, pain interference and participation restriction, and to determine the course of joint pain and disability in community-dwelling adults aged 50 years and over (Thomas et al, 2004b). The study questionnaire (see Appendix 3) contained a set of validated measures designed to collect socio-demographic details and information relating to general health, physical function, participation and bodily pain.

The analysis reported in this thesis was based on the first two phases of the NorStOP study, baseline in 2002 and follow up three years later in 2005. At both time points participants were mailed questionnaires from their general practice, along with an

accompanying letter and a study information leaflet. At each phase, non-responders were sent a reminder postcard after two weeks and a further reminder postcard was sent after two more weeks where necessary (Figure 8.1). Within the final section of the questionnaire, responders were asked to indicate whether they would consent to further contact by the research centre and to provide permission for the research team to access and examine their medical records. Only those participants specifically indicating consent to further contact were sent the follow up questionnaire in 2005. The analysis described in this thesis was based on participants responding to the three year follow up questionnaire who also consented to a medical record review.

Figure 8.1 Flowchart for NorStOP mailing process



The study received ethical approval from the North Staffordshire Local Research Ethics Committee (REC reference numbers 1351, 1430 and 05/Q2604/20).

8.3 NorStOP sampling frame

The population sampling frame was the registered population of six general practices (GP) in North Staffordshire. North Staffordshire has a population of 457,155 (North Staffordshire combined healthcare NHS trust, 2012). The index of multiple deprivation ranks the 32,482 lower super output areas according to multiple measures of deprivation (ranks range from one, most deprived, to 32,482 least deprived) (ONS, 2010). The population sample of the current study represents a broad range of deprivation ratings, from 918 (Practice E) to 18,862 (Practice B) (UK local area). All patients aged 50 years and older within the registered population of these six practices were identified by the Keele General Practice Research Partnership for inclusion in the study.

8.4 NorStOP study questionnaire

The NorStOP survey contained a number of self-completion measures. Measures utilised in the current study (Table 8.1) are described in detail below, including a brief outline of their reliability and validity.

Table 8.1 Measures included in the NorStOP survey

Concept	Measure
Demographic details	
Bodily Pain	Body manikin
Anxiety, Depression	Hospital Anxiety and Depression Scale (HADS)
Sleep problems	Sleep Problem Scale (SPS)
Physical trauma	Medical records
Personal Control	Illness Perceptions Questionnaire Revised (IPQR)
Social networks	Berkman-Syme Social Network Index (BSNI)
Smoking	Single item question
Alcohol use	Single item question

8.4.1 Demographic details

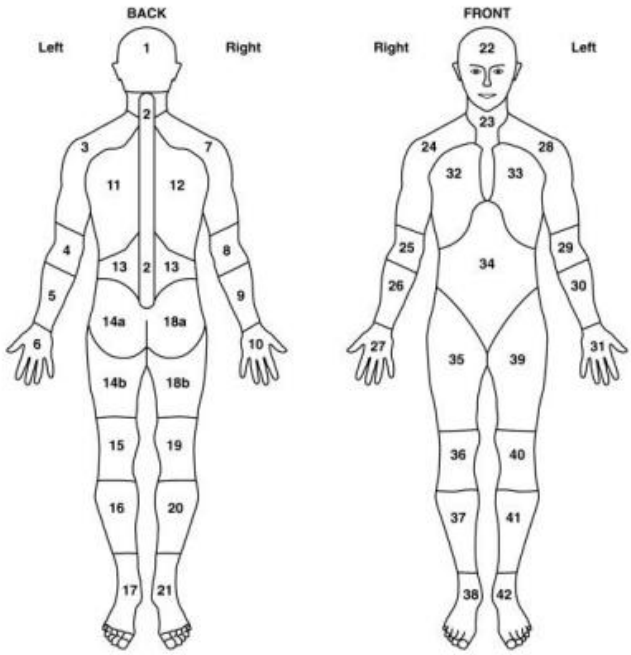
Demographic details including sex, date of birth, marital status, employment status and education were collected. Three groups were used to represent marital status: single, married (including cohabiting), and separated (including divorced or widowed), whilst employment status was classified into four categories: employed, unemployed but

seeking work, not working because of ill health, and other (including housewife or retired). Education was dichotomised based on whether the highest level of education or training was completed up to or after 16 years of age.

8.4.2 Assessment of pain

In both the baseline and follow up surveys, participants were asked “In the past 4 weeks, have you had pain that has lasted for one day or longer in any part of your body?” Those who responded positively were requested to indicate the location of their pain on two blank body manikins depicting the front and back of the body. The participants’ shading was subsequently coded using a template dividing the body into 44 sites, as shown in Figure 8.2. This provided a count of pain sites from zero to 44. As discussed in Section 5.4.2, this is a valid and reliable method of ascertaining the number of painful sites.

Figure 8.2 NorStOP Pain manikin 44 pain sites



8.4.3 Assessment of adult physical trauma

As described in Section 2.2.3c (pg34), individuals with widespread pain often attribute the cause of their symptoms to a physically traumatic experience (Bennett et al, 2007)

and research is suggestive of an association between widespread pain and surgeries (Crombie et al, 1998; Walen et al, 2001; Greenfield et al, 1992; Burckhardt & Jones, 2005), fractures (Castillo et al, 2006; Sanders et al, 2008), RTAs (Holm et al, 2007) and burns (Hamed et al, 2011).

GP read codes were used to identify physically traumatic experiences. Read codes are a "coded thesaurus of clinical terms" (HSC) used in both primary and secondary care. Clinicians use read codes to record details regarding patient visits, symptoms, diagnoses, procedures and test results, onto computerised patient medical records. The information is then used for clinical audits, reporting and in research (NHS Information authority, 2000).

In order to identify physically traumatic experiences from participants' medical records, it was first necessary to compile a list of relevant read codes. Using the NHS browser and the 5 byte access database (November 2011 version 2 supplied by Ian Thomas, Health Informatics) a list of potentially relevant read codes was compiled in consultation with a GP at the Arthritis Research UK Primary Care Centre (Professor Christian Mallen). Read codes are organised in a hierarchical structure, linking multiple "child" (more specific) concepts to a more general parent term. For example, T indicates "cause of injury and poisoning" and T1 "motor vehicle accident", T11 "collision with another motor vehicle", T1100 "motor vehicle driver injured" and T1101 "motor vehicle passenger injured". So whilst over 3,000 individual read codes were found to relate to RTAs, all these items could be identified using ten higher level codes. For each category, the most inclusive, highest level read codes were then identified, as shown in Table 8.2.

Further screening of the read codes for surgeries was carried out to exclude procedures that would not necessarily be construed as traumatic (e.g. "73050 syringe ear to remove wax"). Further consultation with two GPs (Dr Richard Hayward and Dr

Lorna Clarson) was carried out with the criteria of only including codes that would most often result in the patient attending hospital for their surgical procedures.

Table 8.2 Read codes for burns, road traffic accidents, fractures and surgeries

Physical trauma	Read Code	Description
Burns	SH…	Burns and scalds
	TD…	Accidents caused by fire and flames
Road traffic accidents	6927.	RTA injury examination
	9EO..	Road traffic accident claim
	T1…	Motor vehicle traffic accident
	T2…	Motor vehicle non-traffic accident
	T3…	Other road vehicle accident
	TH00.	Late effects of motor vehicle accident
	U0…	Transport, traffic, excluding aircraft, underwater
	U70…	Sequelae of transport accident
	S570.	Neck sprain
	SCW…	Sequelae of unspecified injury of neck and trunk
Fracture	S0…	Fracture of skull
	S1…	Fracture of neck and trunk
	S2…	Fracture of upper limb
	S3...	Fracture of lower limb
	S4…	Fractures and dislocations
	N061.	Traumatic arthropathy
	Syu..	Additional injury and poisoning disease
	82...	Closed reduction of fracture
	8F86.	Convalesc. after fracture Rx
	8HB9.	Fracture therapy follow-up
	9N0X.	Seen in fracture clinic
	N1y1.	Fatigue fracture of vertebra
	N3317	Fracture of bone in neoplastic disease
	N338.	Malunion and nonunion of fracture
	N338z	Fracture malunion or nonunion NOS
	SR1..	Fractures involving multiple body regions
	ZV577	Rehabilitation following fracture
	ZV664	Convalescence after treatment of fracture
	ZV674	Fracture follow-up
Surgery	7….	Operations and procedures
	SP…	Surgical and medical care complications NEC
	TA…	Medical / surgical accidents to patients
	TB…	Medical / surgical accidents to patients - no blame
	U6…	Complications of medical and surgical care

All read codes contain 5 alphanumeric characters. Full stops (.) indicate wildcard characters, for example, all read codes commencing U6 were included

Computerised medical records were then screened for burns, RTAs, surgeries and fractures occurring up to two years prior to the baseline study using these read codes.

8.4.4 Assessment of psychological stress

Psychological stress was assessed using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) and Sleep Problem Scale (Jenkins et al, 1988).

Hospital Anxiety and Depression Scale

As discussed in Section 5.4.4, the HADS (Zigmond & Snaith, 1983) is a reliable and valid measure used to assess anxiety and depressive symptoms experienced by the participant in the previous week.

Sleep Problem Scale

The Sleep Problems Scale (Jenkins et al, 1988) measures how often in the previous four weeks participants experienced four sleep related problems: trouble falling asleep, waking up several times during the night, trouble staying asleep and waking feeling tired. Participants responded “not at all (1)”, “on some nights (2)” or “on most nights (3)” to each question giving a score ranging from 4 to 12, with higher scores indicating greater sleep problems. Research shows that the sleep problem scale has test-retest reliability of 64% (Boardman et al, 2003), good internal consistency (Cronbach’s alpha 0.79) (Jenkins et al, 1988) and construct validity when compared to other sleep / fatigue related scales, such as the Medical Outcome Survey Short Form 36 Vitality subscale (interclass correlation r=-0.7) (Crawford et al, 2010).

8.4.5 Potential mediators

Social support

Social support was assessed using Berkman-Syme Social Network Index (BSNI) (Berkman & Syme, 1979). The index is calculated from participants’ response to seven questions relating to their marital status, number of friends and relatives, the frequency of contact and also their membership of social, community and religious groups. This results in a rating of low, medium, medium / high or high level of social support.

Research using the BSNI has shown that low levels of social support are associated with the interference of pain in daily activities (Peat et al, 2004) and predict nine and seventeen year mortality risks (Berkman & Syme, 1979; Seeman et al, 1987). The BSNI has been shown to be stable over time, with a test retest reliability correlation of r=0.75 over eight years (Kroenke et al, 2006).

Personal Control

The NorStOP survey included four items from the six item personal control subscale of the Illness Perceptions Questionnaire – revised (IPQ-R) (Moss-Morris et al, 2002). Personal control was thus measured using these four items: “There is a lot which I can do to control my health”, “What I do will affect whether my health gets better or worse”, “I have the power to influence what happens in my life” and “The course of my life depends on me”. Participants were asked to rate their agreement with each statement on a five point scale, from “strongly disagree (1)” to “strongly agree” (5). This gives a score ranging from 4 to 20, with higher scores indicating greater personal control. The IPQ-R has good test re-test reliability, predictive and discriminative validity (Moss-Morris et al, 2002). For example, the personal control subscale has a three week test-retest reliability correlation of r=0.57 and good internal consistency (Cronbach alpha 0.81) in rheumatoid arthritis patients (Moss-Morris et al, 2002). The internal consistency of the four questions used in the current study was 0.69 (Cronbach alpha).

8.4.6 Smoking and alcohol use

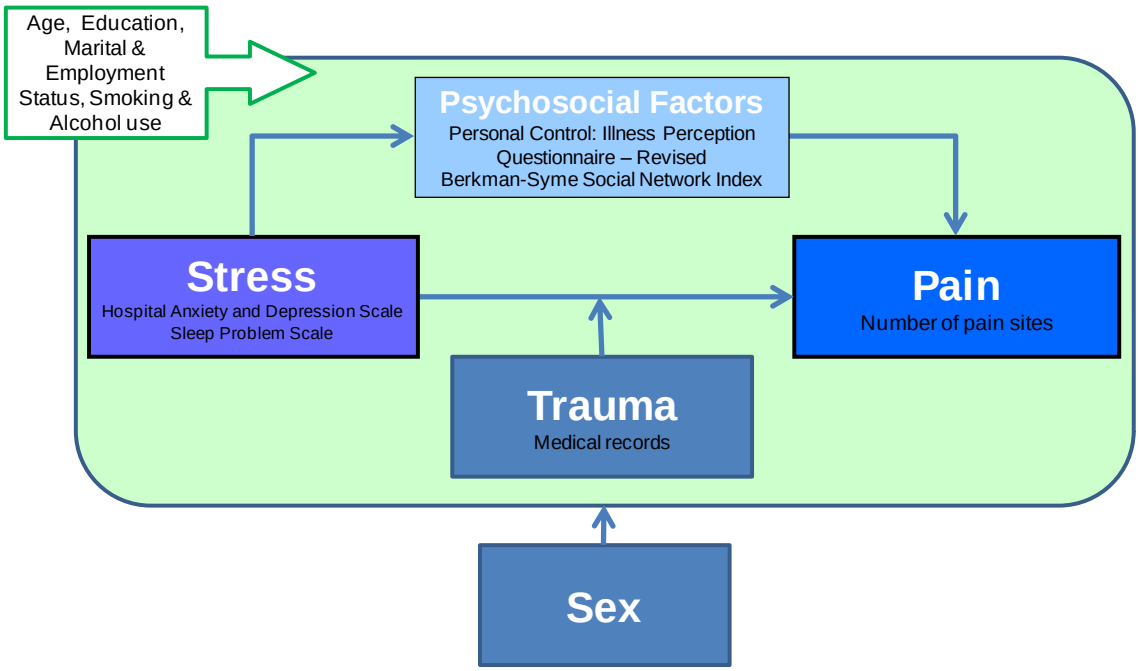
Smoking status was assessed using a single question “What is your current smoking status?” (never smoked, previously smoked, currently smoking). Participants were also asked “On average, how often do you drink alcohol?” (daily / most days, once / twice a week, once / twice a month, once / twice a year, never).

8.5 Statistical analysis and data

The information collected from the above measures was used to compare participants

and non-participants, in the descriptive analysis and to test the adult physical trauma diathesis stress model of widespread pain as described in Sections 4.3, 4.4 and 4.6 respectively. Figure 8.3 shows how the measures described above map onto the adult physical trauma diathesis stress model. Following a description of the outcome, predictor, confounding, moderator and mediator variables, all variables are summarised in Table 8.3.

Figure 8.3 Mapping the measures onto the adult physical trauma diathesis stress model of widespread pain



Outcome variable:

The number of pain sites at follow up was the outcome for this analysis.

Predictor variable:

Confirmatory factor analysis was used to construct a latent variable *psychological stress* by assessing the common variance amongst the observed measures of anxiety, depression and sleep problems at baseline.

Confounding variables:

Smoking status, alcohol use and those demographic variables found to have a significant relationship with the number of pain sites in bivariate analysis were simultaneously added into the stress pain model. Only those variables having a significant relationship with the number of pain sites within the SEM model were retained.

Moderator variables:

Analysis was performed to assess whether the stress pain relationship was moderated by a particular type of physical trauma i.e. surgeries, fractures, RTAs or burns, or by the experience of any physical trauma.

a) **Adult physical trauma types:** Participants were classed as experiencing a physical trauma if their medical records contained any of the trauma related read codes listed in Table 8.2. The four dichotomised variables, surgery, fractures, RTAs and burns, were used in both the bivariate analysis and as moderators in the SEM analysis.

b) **Any physical trauma:** A participant was classed as experiencing any physical trauma if they satisfied the criteria for any of the four physical trauma types (surgery, fractures, RTAs and burns). This dichotomised variable was used in both the bivariate analysis and as a moderator in the SEM analysis.

Mediator variables:

The mediation of the stress pain relationship by personal control was assessed using the total scores from the four questions described above. The mediation by social support was assessed using the four categories of social support (see Table 8.3).

Table 8.3 Summary of outcome, predictor, confounding, moderating and mediating variables for NorStOP analysis

Type	Item	Measure	Range / categories
Outcome	Number of pain sites	Pain manikin	0 – 44
Predictor	*Psychological stress* latent variable	HADS / SPS	
Confounders	Age		50 - 99
	Marital status		Single, married, separated
	Employment status		Working, unemployed, ill, other
	Education beyond 16		Yes / No
Moderators	Sex		Male, Female
	Surgery	Medical records	Yes / No
	Fracture	Medical records	Yes / No
	RTA	Medical records	Yes / No
	Burn	Medical records	Yes / No
	Any trauma	Medical records	Yes / No
Mediator	Personal Control	IPQR-PC	4 - 20
	Social Support	BSNI	Low, medium, medium / high, high

HADS = Hospital Anxiety and Depression Scale; SPS = Sleep Problem Scale; IPQR-PC Illness Perception Questionnaire – Personal Control; BSNI = Berkman-Syme Social Network Index

8.6 Chapter summary

This chapter detailed the methodology of the NorStOP study. Data relating to pain, psychological, social and behavioural factors were collected from a population based sample of males and females at baseline and three year follow up. Information relating to physically traumatic experiences was identified from participants' medical records. The details of how this data were used to assess the trauma diathesis stress model of widespread pain were also provided. The results of the comparison between participants and non-participants are presented in Chapter 9, whilst the results of the descriptive and SEM analysis are presented in Chapter 10.

Chapter 9 The NorStOP study: Comparison of participants and non-participants

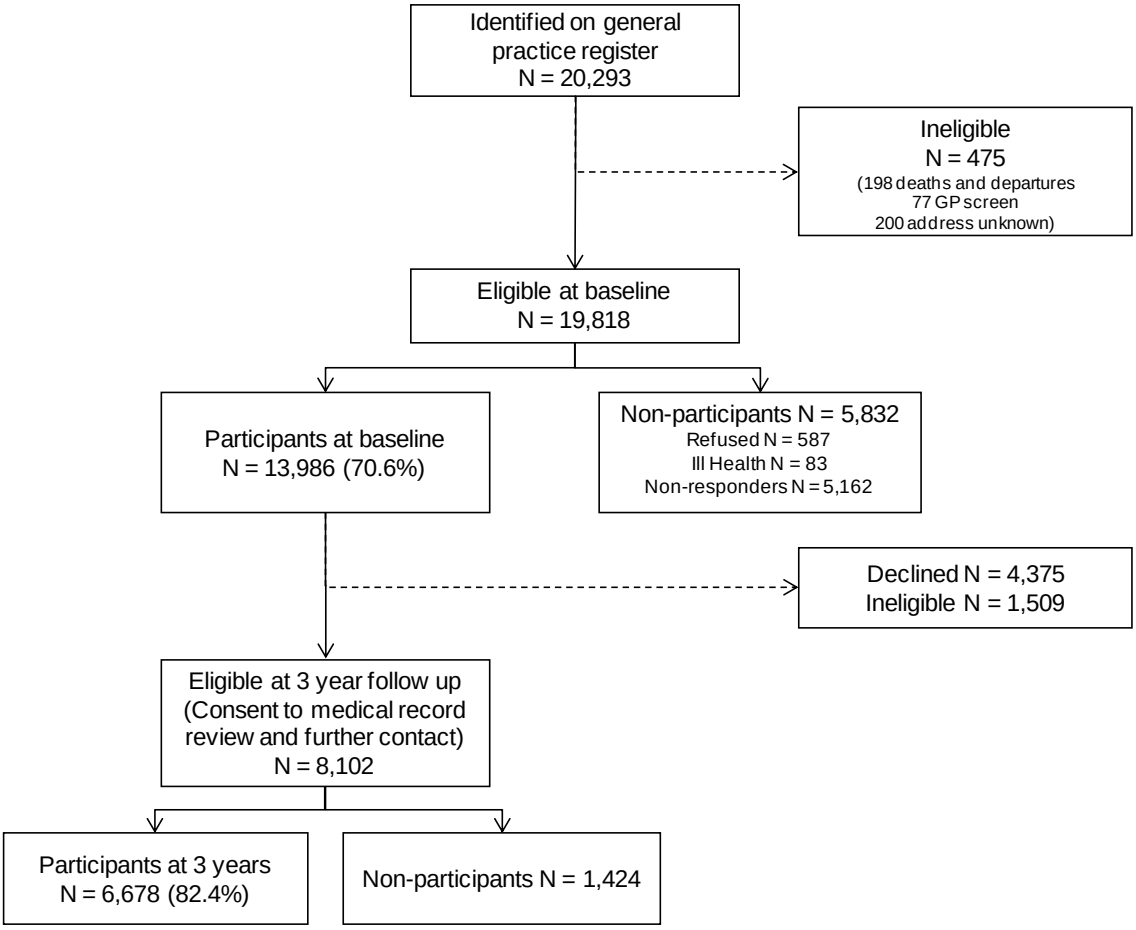
9.1 Chapter overview

This chapter describes the difference between participants and non-participants to the North Staffordshire Osteoarthritis Project (NorStOP) and discusses the implications of such differences for the analysis presented in Chapter 10.

9.2 Participants and non-participants at baseline

Of the 20,293 individuals identified from the general practice registers, 475 (2%) were found to be ineligible (for 200 the address on the general practice register did not match the electoral roll, 198 had died or moved from the practice and 77 were excluded by the GPs). Of the resulting 19,818 eligible individuals who were sent the baseline questionnaire packs, 5,162 (26.0%) failed to respond, 587 (3%) refused to participate and 83 (0.4%) failed to complete the survey due to ill health. This resulted in a study population of 13,986 (70.6%) participants at baseline (see Figure 9.1).

Figure 9.1 Responders and non-responders to NorStOP survey.



Kolmogorov-Smirnov data distribution testing indicated non-normality for all variables; therefore non-parametric tests were used for all bivariate analysis.

Results of the comparisons between participants and non-participants at baseline show that the 13,968 participants were significantly more likely to be females and older than the 5,832 non-participants (Table 9.1). There was also a difference in response rates between the GP practices. Participants were more likely from Practices A and B, and less likely from Practices F and E. Response rates per practice ranged from 64.9% in Practice F to 74.4% in Practice A.

Table 9.1 Characteristics of participants and non-participants at baseline

		Participants (N=13,986)		Non-participants (N=5,832)		P
	IMD	median	IQR	median	IQR	
Age		66	58 – 74	63	56 – 76	**<0.001**[1]
		N	**%**	**N**	**%**	
Male		6,154	66.8	3,059	33.2	**<0.001**[2]
Female		7,832	70.7	3,248	29.3	
Practice A	9,496	2,777	74.4	955	26.6	**<0.001**[3]
Practice B	18,862	1,305	71.0	534	29.0	
Practice C	11,092	2,535	68.6	1,161	31.4	
Practice D	3,067	3,546	68.4	1,636	31.6	
Practice E	918	2,268	65.8	1,181	34.2	
Practice F	8,196	1,555	64.9	840	35.1	

IMD = index of multiple deprivation (1 most deprived, 32,482 least deprived); IQR = interquartile range; N = number; [1]Mann Whitney U test, [2]Chi squared test, [3]Kruskal Wallis Test; significant differences in **red bold**

9.3 Participants and non-participants at thee year follow up

Of the 13,986 participants completing the baseline questionnaire, 8,102 (57.9%) gave permission for their medical records to be reviewed and to be contacted again. The follow up questionnaire three years later was completed by 6,678 (82.4%) of these participants. Results show that compared to non-participants, participants were more likely to be female, older, less likely to be employed or to smoke, were more likely to have continued education beyond age 16 and reported higher levels of social support and personal control. Non-participants reported greater levels of anxiety and depression, and used alcohol less regularly than participants (Table 9.2). There was no significant difference with regard to marital status, sleep problems or number of pain sites at baseline.

Table 9.2 Characteristics of participants and non-participants at follow up

Item	Participants (N=6,678)			Non- participants (N=1,424)			P
	Total	N	%	Total	N	%	
Sex	6,678			1,424			**0.007**[1]
Male		3,041	81.2		704	18.8	
Female		3,637	83.5		720	16.5	
Marital Status	6,609			1,404			0.545[3]
Single		320	82.5		68	17.5	
Married		4,778	82.8		996	17.2	
Separated		1,511	81.6		340	18.4	
Employment Status	6,478			1,375			**<0.001**[3]
Employed		1,964	80.1		487	19.9	
Unemployed		74	82.2		16	17.8	
Not working as ill		481	77.8		137	22.2	
Other		3,959	84.3		735	15.7	
Education	6,584			1,399			**0.038**[1]
Up to age 16		5,837	82.2		1267	17.8	
Post age 16		747	85.0		132	15.0	
Social Support	5,430			1,117			**<0.001**[3]
Low		1,052	78.6		287	21.4	
Medium		2,304	83.2		465	16.8	
Medium / High		730	85.4		125	14.6	
High		1,344	84.8		240	15.2	
Smoking	6,618			1,411			**<0.001**[3]
Never		2,838	84.8		509	15.2	
Previously		2,887	83.2		581	16.8	
Currently		893	73.6		321	26.4	
Alcohol use	6,604			1,408			**0.037**[3]
Daily		1,431	82.6		301	17.4	
1 or 2 per week		2,410	83.1		490	16.9	
1 or 2 per month		1,063	84.2		200	15.8	
1 or 2 per year		1,014	80.4		247	19.6	
Never		686	80.1		170	19.9	
		Median	IQR		Median	IQR	
Age	6,678	64	56 – 71	1,424	61	55 – 72	**0.003**[2]
Anxiety	6,534	6	3 – 9	1,370	7	4 – 9	**0.035**[2]
Depression	6,540	4	2 – 6	1,372	4	2 – 7	**<0.001**[2]
Sleep problems	6,341	7	6 – 9	1,325	8	6 – 9	0.874[2]
Personal control	6,316	16	14 – 16	1,327	15	14 – 16	**0.002**[2]
NPS baseline	6,678	4	0 – 9	1,424	4	0 – 8	0.336[2]

IQR = interquartile range; [1]Chi squared test; [2]Mann Whitney U test; [3]Kruskal Wallis Test; NPS baseline = Number of pain sites at baseline; significant differences in **red bold**

9.4 Discussion

The NorStOP study was a population based longitudinal postal survey of adults aged over 50 years of age. 13,986 (70.6%) participants returned completed questionnaires at baseline, and 6,678 (82.4%) of those also responded to the follow up questionnaire three years later and provided permission for their medical records to be reviewed. This response rate was consistent with rates achieved in studies with similar populations (e.g. Ostbye et al, 2002, 2005). A comparison was made between participants and non-participants at both baseline and follow up in order to assess for potential response bias.

Participants and non-participants at baseline

At baseline, data allowed for comparisons between participants and non-participants with regard to age, sex and general practice. Participants at baseline were more likely to be female and older than non-participants. Both of these factors were considered within the analysis models: age, as a confounding variable, and sex, as a moderator (see Section 10.4); the results are discussed in Section 10.6.

Another potential source of bias could be the difference in participation rate between the general practices. Each general practice was associated with a lower super output area (LSOA) via its postcode, enabling the level of deprivation to be identified. Consistent with previous research, participation was higher from the least deprived areas (Goodman & Gatward, 2008). Area deprivation has been associated with an increased risk of physical ill health and musculoskeletal pain (Urwin et al, 1998; Picket & Pearl, 2001) potentially leading to an underestimation of the prevalence of widespread pain in the current study. Deprivation may also be considered a source of stress (Zhang et al, 2013). However, a relationship between area deprivation and individual psychological stress related factors such as anxiety and depression has not been established (Soomro et al, 2002; Walters et al, 2004). As discussed in Section 6.4, a bias would only be introduced by the difference in deprivation status between participants and non-participants where there was a difference in the relationship between psychological stress and widespread

pain based on deprivation. In order to correctly consider area deprivation, further information would be required, such as how closely the general practice catchment areas correspond to the lower super output areas. Furthermore, the index of multiple deprivation provides a "broad geographical trend" (Harris & Longley, 2002, pg1091) relating to between 1,000 and 3,000 people. This broad trend may not necessarily apply to the individual, potentially leading to further bias (Sedgwick, 2011). The moderation effect of deprivation was not examined within this study, but is a factor worthy of consideration in future research.

Participants and non-participants at follow up

Comparisons were made between participants and non-participants at follow up based on all data collected at baseline. Again, participants were more likely to be female and older than non-participants. No difference was found with regard to sleep problems or the number of pain sites reported at baseline. However, consistent with previous research, (Jones et al, 2011; Volken, 2013) non-participants had reported higher levels of anxiety and depression at baseline than participants. Whilst it is possible that this could lead to an underestimation of any association between these variables and widespread pain, as with the GPSS results reported in Section 6.4, the difference in the medians between those who participated and those who did not are small (Table 9.2) and hence the likely effect would be minimal. Participants also reported higher levels of social support and greater perceived personal control than non-participants. Higher levels of these factors would only detrimentally impact the results of the analysis if the mediation effects of the stress pain relationship were different conditional upon the levels of these factors. However, this seems unlikely as, again, the difference between the participants and non-participants' median scores for personal control was small (Table 9.2) and levels of social support in participants were similar to those reported in other studies (e.g. Kang & Bloom, 1993).

9.5 Chapter summary

This chapter has presented and discussed the differences between participants and non-participants to the NorStOP baseline and three year follow up survey. When considering the external validity, or generalisability, of the study findings it must be noted that the participants were more likely to be female, older, and have GP surgeries in less deprived areas. The participants were also more likely to report higher levels of social support and personal control, and lower levels of anxiety and depression than non-participants. Descriptive and inferential analysis of this data is presented in the following chapter.

Chapter 10 The NorStOP study: Results - Adult trauma, stress and pain

10.1 Chapter overview

This chapter presents the findings from the analysis of the North Staffordshire Osteoarthritis Project (NorStOP) data. An assessment was made of the associations between the number of pain sites and demographic factors, anxiety, depression, sleep problems, social support and personal control. The prevalence of adult physical trauma within the study population is also presented. Structural equation modelling was used to examine the trauma diathesis stress model of widespread pain and the results are presented in Section 10.4. All analysis of the NorStOP data is prospective. The final section of this chapter provides a discussion regarding these findings; including the strengths and limitations of the study and the implications for the trauma diathesis stress model of widespread pain.

10.2 Association between number of pain sites at three year follow up and covariates

This section provides a summary of the characteristics of the 6,678 participants who responded to the three year follow up questionnaire and also provided consent for their medical records to be reviewed.

10.2.1 Number of pain sites

Pain site information was reported by 13,986 participants at baseline. The number of pain sites ranged from 0 to 44 (out of a maximum of 44), with a median of 4 (inter quartile range 0 – 9). No pain was reported by 4,304 (30.8%) participants, with three participants reporting pain in all 44 sites.

Pain site information was provided by 6,677 participants at follow up. The number of pain sites ranged from 0 to 44, with a median of 4 (inter quartile range 0 – 10). No pain

was reported by 1,678 (25.1%) participants, with one participant at follow up reporting pain in all 44 sites. Compared to baseline, 2,266 (33.9%) participants had pain in the same number of sites plus or minus one pain site; 2,337 (35%) participants had pain in fewer sites, 1,326 (20%) had pain in the same number of sites and 3,014 (45%) reported pain in more sites at three year follow up. Of the 4,304 participants reporting no pain at baseline, 1,827 completed the follow up survey and 949 (51.9%) of those continued to report no pain at follow up.

10.2.2 Participant characteristics and association with number of pain sites

As shown in Table 10.1, the number of pain sites at three year follow up was significantly higher for those participants who were female, separated, divorced or widowed, not working due to ill health, those who had not pursued education beyond age 16 years, who currently smoked, and those who had never used alcohol.

In the two years prior to baseline data collection, surgery, fractures, RTAs and burns were recorded in 668 (10%), 130 (1.9%), 69 (1.0%) and 17 (0.3%) of participants' medical records, respectively. Taken together, 840 (12.6%) participants had experienced one or more of these traumatic events. Whilst there was no difference in the occurrence of trauma between males and females (p=0.796), participants with a trauma on their medical records were older than those without (trauma median age 65 IQR 57-73, no trauma median age 64 IQR 56-71, p=0.03). When considering the individual types of physical trauma, the number of pain sites was significantly higher for participants with surgery and / or fractures, but not RTAs or burns. The occurrence of any physical trauma was significantly associated with an increase in the number of pain sites (p=0.001).

Table 10.1 Participant characteristics by number of pain sites

Item		Total*	N	%	Pain Sites at 3 Year follow up		P
					Median	IQR	
Sex		6,677					**<0.001**[1]
Male			3,041	45.5	4	0 – 9	
Female			3,636	54.5	5	1 – 11	
Marital Status		6,608					**<0.001**[2]
Single			320	4.8	3	0 – 8	
Married			4,777	72.3	4	1 – 10	
Separated			1,511	22.9	5	1 – 11	
Employment Status		6,477					**<0.001**[2]
Employed			1,964	30.3	4	0 – 8	
Unemployed			74	1.2	5	0 – 10	
Not working as ill			481	7.4	11	5 – 19	
Other			3,958	61.1	4	0 –10	
Education		6,583					**<0.001**[1]
Up to age 16			5,836	88.7	5	0 – 10	
Post age 16			747	11.3	2	0 – 6	
Social Support		5,429					0.101[2]
Low			1,052	19.4	5	1 – 11	
Medium			2,304	42.4	4	0 – 10	
Medium / High			730	13.4	4	0 – 9	
High			1,343	24.8	5	1 – 10	
Smoking		6,617					**0.001**[2]
Never			2,837	42.9	4	0 – 10	
Previously			2,887	43.6	5	1 – 10	
Currently			893	13.5	5	1 – 11	
Alcohol use		6,603					**<0.001**[2]
Daily			1,431	21.7	4	0 – 8	
1 or 2 per week			2,410	36.5	4	0 – 9	
1 or 2 per month			1,063	16.1	4	0 – 11	
1 or 2 per year			1,014	15.3	5	1 – 11	
Never			685	10.4	6	2 – 13	
Physical trauma		6,677					
Surgery	Yes		668	10.0	5	1 – 11	**0.024**[1]
	No		6,009	90.0	4	0 – 10	
Fracture	Yes		130	1.9	7	2 – 14	**0.010**[1]
	No		6,547	98.1	4	0 – 10	
RTA	Yes		69	1.0	5	2 – 9	0.847[1]
	No		6,608	99.0	4	0 – 10	
Burns	Yes		17	0.3	4	0 – 10	0.242[1]
	No		6,660	99.7	5	3 – 15	
Any trauma	Yes		840	12.6	5	1 – 11	**0.001**[1]
	No		5,837	87.4	4	0 – 10	

Total = Total number of participants responding; IQR = inter quartile range; [1]Mann-Whitney U Tests; [2]Kruskall-Wallis test; RTA = road traffic accident, Any trauma includes surgery, fractures, RTAs and burns; significant differences in **red bold**

As shown in Table 10.2, significant positive correlations were found between anxiety, depression and sleep problems and between these three variables and the number of pain sites at baseline and follow up. Personal control was significantly and negatively

associated with anxiety, depression, sleep problems and number of pain sites at baseline and follow up. The participants were aged between 50 to 90 years (median 64 for both males and females). Age was significantly associated with depression (positive), anxiety and personal control (negative). Negative correlations were also found between age and number of pain sites at baseline and follow up, although these failed to reach significance.

Table 10.2 Pearson correlations for anxiety, depression, sleep, personal control, age and number of pain sites at baseline and 3 year follow up

	Anxiety	Depression	Sleep Problems	Personal control	Age	NPS Baseline
Anxiety	1					
Depression	**0.653****	1				
Sleep problems	**0.502****	**0.477****	1			
Personal control	**-0.213****	**-0.286****	**-0.187****	1		
Age	**-0.082****	**0.057****	0.004	**-0.056****		
NPS baseline	**0.300****	**0.366****	**0.367****	**-0.132****	-0.010	
NPS follow up	**0.287****	**0.338****	**0.338****	**-0.135****	-0.021	**0.660****

Significant correlations in **red bold; ** Correlation is significant at the 0.01 level (2-tailed);
NPS = number of pain sites

10.3 Missing data

Although overall missing data was less than 5% per item (criteria for acceptability as discussed in Section 4.5) the accumulative effect of full case analysis would result in a 32.4% loss in sample size at three year follow up. Little's MCAR test (see Section 4.5) showed data to be completely missing at random. Data was therefore imputed for those 2,163 participants with missing data.

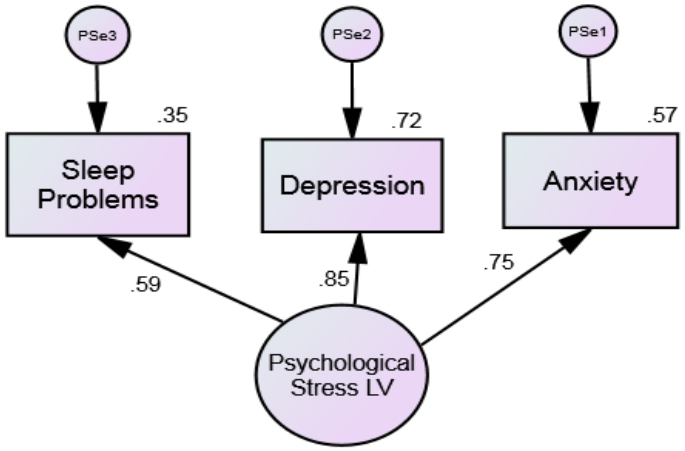
10.4 Structural equation modelling

These results are based on 6,678 participants, with imputed data as described above.

10.4.1 Stress and pain

The *psychological stress* latent variable (Figure 10.1) was a good fit to the baseline data (SRMR ≤0.026). Although the RMSEA was higher than the recommended level of 0.06 (see Section 4.6), each of the observed measures had a statistically significant relationship with the *psychological stress* latent variable. Table 10.3 shows the standardised (β) and unstandardised regression (B) coefficients for the psychological stress latent variable.

Figure 10.1 Psychological stress latent variable



Root mean square error of approximation (RMSEA) = 0.132
Standardised root mean square residual (SRMR) = 0.0260

PSe1-3 - error terms for anxiety, depression and sleep problems; LV = latent variable; numbers on arrows from latent variable = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

Table 10.3 Regression coefficients for psychological stress latent variable

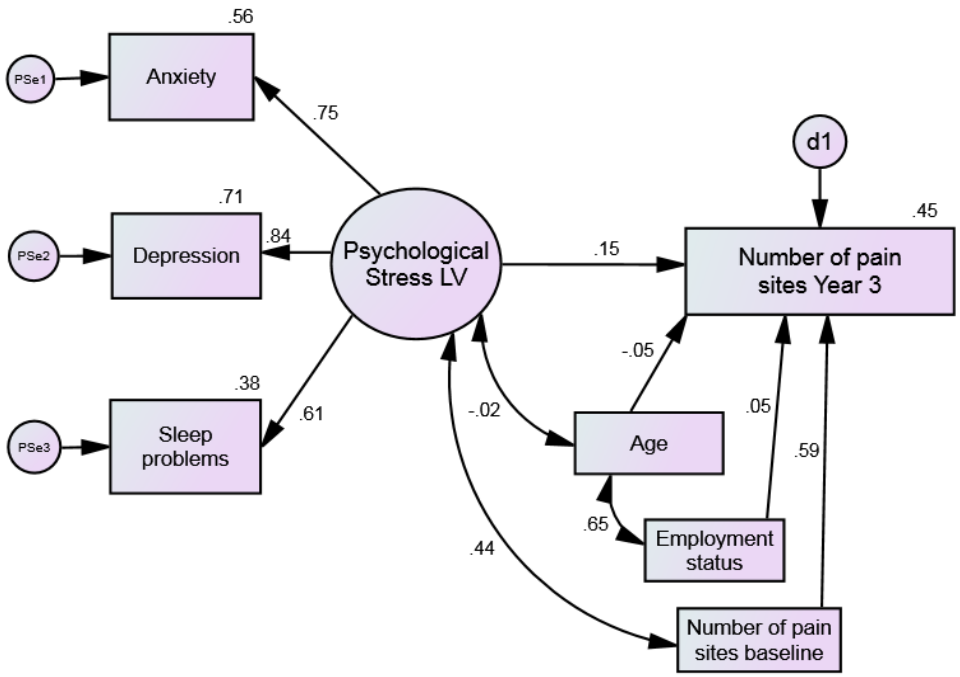
Observed Variable	β	95% C.I.		B	95% C.I.		R^2
Anxiety	0.754	0.742	0.766	1	1	1	0.569
Depression	0.853	0.837	0.861	1	1	1	0.721
Sleep problems	0.594	0.574	0.616	0.434	0.414	0.454	0.353

β = Standardised regression coefficient; B = Unstandardised regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation

Based on previous research and the findings of significant associations with the number of pain sites in the bivariate analysis (see Section 10.3.2 above), age, education,

employment and marital status, smoking and alcohol use were considered as potential confounders of the stress pain relationship (as described in Section 4.6.2). The SEM analysis showed no significant relationship between the number of pain sites and education (p = 0.483), marital status (p = 0.934), smoking (p=0.438) and alcohol use (p=0.151). Only age and employment status were found to have a significant contribution (p=0.001) and so were retained as confounding variables in the final model (as shown in Figure 10.2). The *psychological stress* latent variable, created from baseline levels of anxiety, depression and sleep problems, had a statistically significant relationship with the number of pain sites at 3 year follow up (β = 0.15, p<0.001). The model explained 45% of the variance in the number of pain sites.

Figure 10.2 Psychological stress and number of pain sites controlling for age and employment status



Root mean square error of approximation (RMSEA) = 0.032
Standardised root mean square residual (SRMR) = 0.0436

PSe1-3 - error terms for anxiety, depression and sleep problems; d1 = disturbance term for number of pain sites at follow up; LV = latent variable; numbers on arrows = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

10.4.2 Stress and pain: moderation by adult physical trauma

Using the model from Figure 10.2, the moderation effects of surgery, fracture and RTAs were tested separately. An independent assessment of the moderation effect of burns was not possible due to the small number of occurrences (see Table 10.1). "Any trauma" includes all four physical trauma types (surgery, fracture, RTAs and burns). Table 10.4 shows the regression coefficients for the stress pain relationship firstly for all participants, for each physical trauma type and then for any physical trauma. The stress pain relationship was significantly stronger for individuals without any physical trauma compared to those with any physical trauma (β 0.157 compared to β 0.100 $p<0.05$). The stress pain relationship was not significant for those participants with fractures and RTAs.

Table 10.4 Psychological stress and number of pain sites moderated by individual adult physical trauma types

Adult physical trauma type		N	%	β	95% CI		B	R^2	Comparison
All		6,678		0.149	0.124	0.174	0.379	0.452	
Surgery	No	6,010	85.9	0.155	0.129	0.181	0.402	0.450	Referent
	Yes	668	14.1	0.108	0.030	0.179	0.240	0.477	1.917
Fracture	No	6,548	98.1	0.149	0.123	0.175	0.379	0.451	Referent
	Yes	130	1.9	0.145	-0.029	0.301	0.332	0.465	0.256
RTA	No	6,609	99.0	0.151	0.127	0.177	0.386	0.453	Referent
	Yes	69	1.0	-0.038	-0.301	0.309	-0.075	0.408	1.902
Any trauma	No	5,838	87.4	0.157	0.130	0.185	0.409	0.452	Referent
	Yes	840	12.6	0.100	0.026	0.164	0.226	0.456	**2.341***

β = Standardised regression coefficient for psychological stress to pain relationship; B = Unstandardised regression; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B; RTA = road traffic accident; Any trauma includes surgery, fracture, road traffic accident and burns; significant values in **red bold;** *p value <0.05

10.4.3 Stress and pain: moderation by adult physical trauma and sex

Due to the small number of participants who had experienced the individual physical trauma types, moderation by sex was restricted to assessing the effect of any physical trauma. The stress pain relationship was not significant for males who had experienced

any physical trauma (p=0.091). The strength of the relationship was not significantly different when comparing males to females (critical ratio = 0.351), males with and without trauma (critical ratio = 1.828) or females with and without trauma (critical ratio = 1.546) (see table 10.5).

Table 10.5 Psychological stress and number of pain sites moderated by adult physical trauma and sex

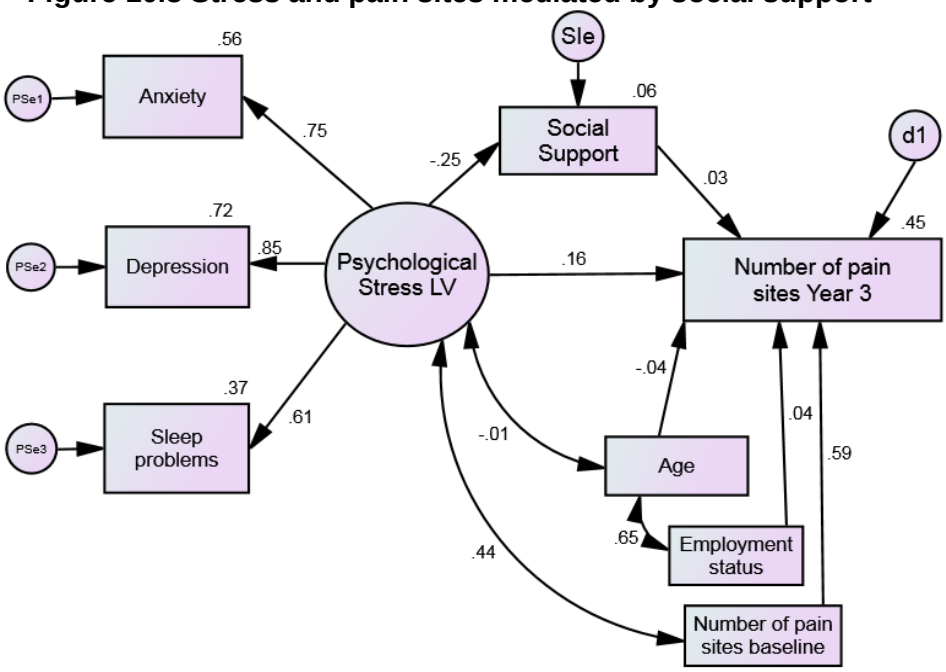
Group		N	%	β	95% CI		B	R^2	Comparisons
Males	All	3,041		0.153	0.116	0.192	0.358	0.419	
	No trauma	2,655	87.3	0.166	0.124	0.208	0.389	0.404	Referent
	Any trauma	386	12.7	0.080	-0.012	0.173	0.187	0.504	1.828
Females	All	3,637		0.141	0.107	0.176	0.378	0.468	
	No trauma	3,183	87.5	0.148	0.113	0.184	0.410	0.477	Referent
	Any trauma	454	12.5	0.111	0.019	0.206	0.432	0.416	1.546

β = Standardized regression coefficient; B = Unstandardised regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; R^2 = multiple squared correlation for number of pain sites; Comparison = critical ratios for differences between B; Any trauma includes surgery, fracture, road traffic accident and burns; significant values in **red bold;** *p value <0.05

10.4.4 Stress and pain: Mediation by social support and personal control

The trauma diathesis stress model of widespread pain proposed personal control and social support as potential pathways through which stress might influence widespread pain. Two mediation models were created by adding social support and personal control to the model depicted in Figure 10.2. An example of the resulting models is shown in Figure 10.3. The stress pain relationship was mediated by social support (indirect effects β = -0.007, p = 0.006, R^2 = 0.45 – Table 10.6), but not by personal control (indirect effects β = 0.002, p = 0.496, R^2 = 0.45 – Table 10.6).

Figure 10.3 Stress and pain sites mediated by social support



Root mean square error of approximation (RMSEA) = 0.018
Standardised root mean square residual (SRMR) = 0.0444

PSe1-3 - error terms for anxiety, depression and sleep problems; d1 = disturbance term for number of pain sites; Sle – disturbance term for social support; LV = latent variable; numbers on arrows = standardised beta coefficients; numbers above observed variables = multiple squared correlation (variance explained).

Table 10.6 Psychological stress and number of pain sites mediated by social support and personal control

Mediator		β	95% CI		P	B	R^2	a	b
Social Support	Indirect	-0.007	-0.012	-0.002	**0.006***	-0.018	0.452	-0.254	0.028
	Direct	0.156	0.130	0.180	0.001	0.395		(-0.277, -0.230)	(0.009, 0.046)
	Total	0.149	0.124	0.173	0.001	0.377			
Personal control	Indirect	0.002	-0.004	0.010	0.496	0.006	0.452	-0.324	-0.007
	Direct	0.146	0.119	0.171	0.001	0.370		(-0.352, -0.296)	(-0.029, 0.014)
	Total	0.148	0.123	0.172	0.001	0.376			

Analysis based on 6,678 participants; β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardised regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical p value <0.05; significant values in **red bold**

10.4.5 Stress and pain: Moderated mediation

The two mediation models examined in the previous section were next assessed to identify any moderation effects of adult physical trauma and sex.

a) Moderation by adult physical trauma

The mediation of the stress pain relationship by social support was not moderated by the experience of trauma; the indirect effects were significant regardless of trauma status (Table 10.7). The stress pain relationship was not mediated by personal control even when examining the no trauma and any trauma groups individually (Table 10.8).

b) Moderation by adult physical trauma and sex

The mediation of the stress pain relationship by social support was not moderated by physical trauma and sex. For males who had experienced any trauma, the stress pain relationship was not significant (see Table 10.5). Although psychological stress did not predict the number of pain sites, there was an indirect effect through social support (Table 10.9). The indirect effects were not significant for females with or without any physical trauma (Table 10.9).

The stress pain relationship was not mediated by personal control even when examining the no trauma and trauma groups separately by sex (Table 10.10).

Table 10.7 Psychological stress and number of pain sites mediated by social support and moderated by physical trauma

		β	95% CI		P	B	R^2	a	b	Model fit	
No trauma	Indirect	-0.006	-0.011	-0.001	**0.016**	-0.015	0.451	-0.262	0.022	RMSEA	0.021
	Direct	0.163	0.164	0.191	0.001	0.421		(-0.287, -0.236)	(0.004, 0.041)	SRMR	0.0444
	Total	0.157	0.128	0.183	0.001	0.406					
Any trauma	Indirect	-0.015	-0.030	-0.005	**0.004**	-0.034	0.459	-0.200	0.075		
	Direct	0.119	0.051	0.191	0.002	0.267		(-0.266, -0.130)	(0.021,0.130)		
	Total	0.104	0.037	0.172	0.002	0.233					

Analysis based on 6,678 participants; Any trauma = 840 (12.6%); β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardised regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical p value <0.05; significant indirect effects in **red bold**

Table 10.8 Psychological stress and number of pain sites mediated by personal control and moderated by physical trauma

		β	95% CI		P	B	R^2	a	b	Model fit	
No trauma	Indirect	0.004	-0.004	0.011	0.324	0.010	0.452	-0.321	-0.012	RMSEA	0.019
	Direct	0.153	0.124	0.183	0.001	0.396		(-0.350, -0.292)	(-0.034, 0.013)	SRMR	0.0422
	Total	0.157	0.128	0.183	0.001	0.406					
Any trauma	Indirect	-0.007	-0.029	0.013	0.473	-0.015	0.456	-0.337	0.020		
	Direct	0.107	0.037	0.183	0.003	0.241		(-0.407, -0.260)	(-0.039, 0.082)		
	Total	0.100	0.033	0.169	0.003	0.225					

Analysis based on 6,678 participants; Any trauma = 840 (12.6%); β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardised regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical p value <0.05; significant indirect effects in **red bold**

Table 10.9 Psychological stress and number of pain sites mediated by social support and moderated by physical trauma and sex

			β	β 95% CI		P	B	R^2	a	b	Model fit	
Males	No trauma	Indirect	-0.009	-0.017	0.000	0.051	-0.020	0.403	-0.267	0.032	RMSEA	0.018
		Direct	0.174	0.130	0.216	0.001	0.407		(-0.304, -0.229)	(-0.001, 0.061)	SRMR	0.0573
		Total	0.166	0.124	0.206	0.001	0.387					
	Any trauma	Indirect	-0.015	-0.037	-0.003	**0.008**	-0.035	0.508	-0.156	0.097		
		Direct	0.103	0.005	0.198	0.040	0.238		(-0.254, -0.050)	(0.019, 0.177)		
		Total	0.088	-0.008	0.183	0.072	0.203					
Females	No trauma	Indirect	-0.004	-0.011	0.003	0.235	-0.011	0.477	-0.260	0.016		
		Direct	0.151	0.116	0.187	0.001	0.417		(-0.295, -0.226)	(-0.012, 0.041)		
		Total	0.147	0.112	0.182	0.001	0.406					
	Any trauma	Indirect	-0.012	-0.035	0.005	0.148	-0.027	0.417	-0.239	0.052		
		Direct	0.124	0.027	0.222	0.015	0.270		(-0.326, -0.149)	(-0.026, 0.128)		
		Total	0.111	0.015	0.206	0.027	0.243					

Analysis based on 6,678 participants: Males = 3,041; Any trauma = 386 (12.7%). Females = 3,637; Any trauma = 454 (12.5%). β = Bias corrected confidence intervals based on bootstrap of 3000; B= Unstandardised regression coefficient; R^{2-} multiple squared correlation;; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical p value <0.05; significant indirect effects in **red bold**

Table 10.10 Psychological stress and number of pain sites mediated by personal control and moderated by physical trauma and sex

			β	β 95% CI		P	B	R^2	a	b	Model fit	
Males	No trauma	Indirect	0.007	-0.003	0.017	0.175	0.017	0.404	-0.322	-0.023	RMSEA	0.022
		Direct	0.154	0.134	0.174	0.001	0.362		(-0.366, -0.279)	(-0.053, 0.010)	SRMR	0.0423
		Total	0.162	0.141	0.183	0.001	0.379					
	Any trauma	Indirect	-0.028	-0.065	0.001	0.058	-0.066	0.511	-0.392	0.072		
		Direct	0.155	0.127	0.186	0.001	0.362		(-0.492, -0.282)	(-0.005, 0.144)		
		Total	0.126	0.086	0.168	0.001	0.295					
Females	No trauma	Indirect	0.001	-0.008	0.011	0.803	0.003	0.477	-0.298	-0.004		
		Direct	0.146	0.108	0.184	<0.001	0.402		(-0.336, -0.258)	(-0.037, 0.026)		
		Total	0.147	0.113	0.184	<0.001	0.405					
	Any trauma	Indirect	0.003	-0.021	0.029	0.818	0.006	0.416	-0.285	-0.010		
		Direct	0.108	0.013	0.209	0.001	0.235		(-0.392, -0.183)	(-0.095, 0.075)		
		Total	0.110	0.019	0.206	0.001	0.241					

Analysis based on 6,678 participants: Males = 3,041; Any trauma = 386 (12.7%). Females = 3,637; Any trauma = 454 (12.5%). β = Bias corrected confidence intervals based on bootstrap of 3000; B= Unstandardised regression coefficient; R^{2-} multiple squared correlation;; a = path from psychological stress to mediator; b = path from mediator to number of pain sites; critical p value <0.05; significant indirect effects in **red bold**

10.5 Discussion

This section provides a summary of the findings from the NorStOP study and a comparison to previous studies. The trauma diathesis stress model of widespread pain was assessed by progressively more complex models; interpretations of the findings from each model are discussed in turn. Following an examination of the strengths and limitations of the study, the implications of the findings for the trauma diathesis stress model of widespread pain are presented.

10.5.1 Summary of findings

The aim of the analyses presented in this chapter was to ascertain whether the experience of a physical trauma in adulthood increased the risk that psychological stress would lead to widespread pain. The physical traumas examined were surgery, fracture, road traffic accidents (RTAs) and burns. To summarise, the results offer partial support for the trauma diathesis stress model of widespread pain proposed in Section 2.5 (pg50) and the hypotheses presented in Chapter 3:-

(1) Among adults, an increase in psychological stress was associated with an increase in the number of pain sites.

(2) The relationship between psychological stress and number of pain sites was moderated by exposure to adult physical trauma, but not by sex. The stress pain relationship was not moderated by any individual physical trauma type. However, the stress pain relationship was significantly stronger in those individuals who did not have any physical trauma recorded on their medical records compared to those who did.

(3) The relationship between psychological stress and number of pain sites was mediated by social support, but not by personal control.

(4) The mediation of the stress pain relationship by social support was not moderated by adult physical trauma or by sex.

10.5.2 Comparison with previous studies

No studies have been identified which specifically report the number of sites of pain using the 44 site pain manikin; however, comparisons can be made with other studies using a pain site count. For example, using a count of nineteen pain sites, Hauser et al (2012) found that 24.5% of their 60 to 85 year old community based population reported no pain and 10.1% had pain in one site. This seems consistent with the findings of the current study (25.1% no pain and 12.3% pain in two out of 44 sites at follow up). Also 1,326 (20%) of participants in the current study reported pain in the same number of pain sites at baseline and follow up, which is similar to the 17% reported in Kamaleri et al's (2009) community based study.

Female participants reported a significantly higher number of pain sites than males at three year follow-up, which was consistent with previous studies (e.g. Kamaleri et al, 2008b; Svebak et al, 2006), but not all (e.g. Gupta et al, 2007; Jones et al, 2011; GPSS study). As described in Section 1.4.1, Table 1.1 (pg8), previous research has suggested that the prevalence of widespread pain decreases with age. For example, Svebak et al (2006) found that the prevalence of widespread pain decreased in females from age 50-59 years and in males from age 60-69. The current study found a negative trend overall (both males and females), although this was not significant ($r=-0.021$, $p=0.083$). Further examination of the correlation between age and number of pain sites by sex showed a significant effect for males ($r=-0.039$. $p=0.032$) but not for females ($r=-0.012$, $p=0.472$). This would suggest that the number of pain sites decreases with age as a trend, but more so for males (median age 64 years).

The median scores for anxiety and depression for the current study were consistent with previous research within general population samples (Crawford et al, 2001). In a community study Kang et al (1993) assessed social support using the BSNI in participants aged over 55 years. They found that 13%, 48%, 13% and 26% reported low, medium, medium / high and high levels of support, respectively, rates similar to those in

the current study (19%, 43%, 13%, 25%, respectively). The incidence of adult physical trauma was less than has been reported in other studies and in national statistics. The obtained annual incidence rates were 5% for surgery, 1.0% for fractures, 0.5% for RTAs and 0.2% for burns in the study population, compared to annual rates of 7% (Royal College of Surgeons, 2012), 3.6% (Donaldson et al, 2008), 1.2% (Department of Transport, 2013a) and 0.3% (McCormick et al, 1995), respectively. However, these lower incidence rates are likely to be due to the age of the NorStOP participants (median age 64 years). As described in Section 2.2.3, surgeries, RTAs and burns decrease with age (Royal College of Surgeons, 2012; Department of Transport, 2013b; McCormick et al, 1995), although rates for fractures increase from age 55 years in females (Donaldson et al, 2008).

As suggested by previous research, in the bivariate analysis the number of pain sites was positively associated with marital status, employment status, education and smoking (Kamaleri et al, 2008b; Viniol et al, 2013; Bergman, 2005; VanDenKerkhof et al, 2011) and negatively associated with alcohol use (Bergman et al, 2002). When these factors were included within the SEM model, only age and employment status were found to have a significant contribution and so were retained as confounders.

Overall, the findings of the current study with regard to the number of pain sites, levels of anxiety and depression, and the incidence of adult physical trauma are consistent with findings from previous studies. As this suggests that these findings are independent of the study population, the results may generalisable to the general population.

10.5.3 Interpretation of SEM findings

a) Stress and pain

Confirmatory factor analysis was used to create a *psychological stress* latent variable by assessing the common variance amongst the observed variables for anxiety, depression and sleep problems. No previous research has been identified which

specifically combined sleep problems, anxiety and depression into a latent variable, but other studies have found significant correlations between these three factors (Specchio et al, 2004; Eller et al, 2006). The *psychological stress* latent variable was used to assess the relationship between stress and number of pain sites in the SEM model depicted in Figure 10.2. An increase in psychological stress was significantly associated with an increase in the number of pain sites ($\beta = 0.15$, $p=0.001$). The model was a good fit to the data and explained 45% of the variance in the number of pain sites. Whilst the three factors of anxiety, depression and sleep problems have been consistently associated with widespread pain in cross-sectional and prospective analysis (for example, Gupta et al, 2007; Davies et al, 2008; as detailed in Section 2.3.2), this was the first time the relationship had been assessed using all three factors combined in a latent variable. A comparison of effect size from previous studies is therefore difficult, although these results are consistent with those in the GPSS prospective analysis, which used anxiety, depression, somatisation and life events to assess psychological stress. These results demonstrate the importance of psychological stress in the development and persistence of widespread pain.

b) Stress and pain: moderation by adult physical trauma

(i) Individual adult trauma types

As detailed in Section 8.5 (pg187), the moderation effect on the stress pain relationship of each individual trauma type was assessed. Although surgeries and fractures were significantly associated with the number of pain sites in the bivariate analysis, there was no significant moderation effect for any of the individual types of trauma in the SEM analysis. The stress pain relationship was not significant for those participants with fractures or those with RTAs recorded on their medical records. This may be due to the small number of these events, as indicated by the wide confidence intervals, especially for RTAs.

(ii) Any adult trauma

An assessment was also made of the moderation effect of the experience of any trauma. The stress pain relationship was significantly stronger for those individuals without ($\beta = 0.16$) compared to those with ($\beta = 0.10$) a trauma recorded in their medical records ($p=0.02$). This was contrary to the prediction of the trauma diathesis stress model of widespread pain.

The results for the individual trauma types and any trauma suggest that surgeries, fractures, RTAs and burns in adulthood do not increase an individual's susceptibility to widespread pain when they become stressed. Alternatively, this lack of moderation effect may be due to the inclusion of non-traumatic events (dilution effect), because those individuals who experienced a trauma received treatment or because only a direct association exists between physical trauma and widespread pain. These potential explanations are discussed in turn.

Firstly, it is possible that only certain types of surgery, fractures, RTAs and burns confer a susceptibility to psychological stress and widespread pain and by including all of these events the effect has been diluted and weakened. For example, is the surgical removal of a tooth more or less traumatic than a hip replacement? And would a fracture of the little toe be as traumatic as a spinal column fracture? Clearly there is heterogeneity among the included read codes. The challenge would be to identify which surgeries, fractures, RTAs and burns, if any, do increase susceptibility to widespread pain. Alternatively, it may not be the occurrence of such events that increases susceptibility to widespread pain; it may be the individual's reaction to the event. Secondly, as the trauma was detailed in the patients' medical records, it is possible and likely that some form of treatment had been received. It may be that the treatment addressed or prevented any psychological stress or widespread pain.

Thirdly, it could be argued that physical traumas are more likely to lead directly to pain, potentially via central sensitisation, rather than by increasing susceptibility to widespread pain via psychological stress. This may explain the lack of moderation. However, as the results show, RTAs and burns were not significantly associated with the number of pain sites in the bivariate analysis (Table 10.1) and the research reviewed in Section 2.5.3c (Table 2.2, pg34) shows very little evidence for such a direct relationship. The results of the current study are consistent with the results of previous prospective research. Of the prospective studies identified, widespread pain was directly associated with RTAs in only one (of five) studies. No studies found a significant association between widespread pain and fractures (out of four studies) or surgeries (one study). In both the Wynne-Jones et al (2006a) and Jones et al (2011) studies, psychological stress had explained some of the relationship between RTAs and widespread pain. It had been anticipated that by examining the relationship in a different way, with psychological stress as the predictor and trauma as the moderator, the relationship between these factors would be clarified. However, this was not the case. Adult physical trauma did not increase an individual's susceptibility to the subsequent development of widespread pain when they become stressed.

c) Stress and pain: moderation by adult trauma and sex

The stress pain relationship was not moderated differently for males and females. The results showed a trend (although not signficiant) for the stress pain relationship to be stronger in those individuals without a trauma on their medical records, compared to those with a trauma on their medical records for both males and females. The stress pain relationship was not significant for males who had a trauma recorded on their medical records.

d) Stress and pain: mediation by psychosocial factors

As hypothesised, social support showed a significant mediating effect on the stress pain relationship, although the effect was small. Higher levels of social support seemed

to provide some protection from the effects of stress, reducing the risk of an increase in the number of pain sites. Such stress “buffering” effects of social support have long been identified (Cohen & Wills, 1985, pg310). Social support has been associated with decreased physiological reactions to stress, including decreased levels of cortisol during stress (Ditzen et al, 2008; Heinrichs et al, 2003) and improved immune functioning (Loucks et al, 2006). Behaviourally, social support has been associated with health promoting behaviours such as increased physical activity (Warner et al, 2011), smoking cessation (Berkman et al, 2000) and attendance at health screening tests (Muliira & Musil, 2010). Psychologically, high levels of social support have also been associated with high levels of self-efficacy (Warner et al, 2011) and self-esteem (Schroevers et al, 2003), and the use of effective coping strategies which have also been shown to reduce the stress response (Mausbach et al, 2011). These physiological, behavioural and psychological benefits of higher levels of social support may have reduced the risk of widespread pain.

There was a significant difference in the levels of depression, anxiety and sleep problems between participants reporting high and low levels of social support. This could be attributed to mood congruent recall (Kawachi & Berkman, 2001) as individuals with high levels of psychological stress may under report the support they receive (Forgas et al, 1984). The participants’ responses to the BSNI may thus reflect perceived rather than actual levels of social support.

Personal control refers to the level of control an individual perceives themselves to have over their lives. In the current study, two of the four questions related specifically to control over health (as described in Section 8.4.5, pg186). Personal control was negatively correlated with psychological stress (anxiety, depression and sleep problems), and the number of pain sites at both baseline and follow up (Table 10.1). As levels of personal control increased, levels of psychological stress decreased and so did the number of sites of pain. This would indicate that individuals with higher levels of

personal control experience less psychological stress and pain in fewer sites than individuals with lower levels of personal control. However, no mediation of the stress pain relationship was found. This may be because there is no mediation effect to find, or because of a problem with the measurement or analysis of this information. Data relating to only four of the six items within the personal control scale of the IPQ-R had been collected as part of the NorStOP study. Whilst this makes comparisons with previous studies difficult, it is also possible that this has compromised the validity and reliability of the scale. As with the mediator variables within the GPSS analysis, both social support and personal control were measured at baseline, which is not ideal for mediation analysis (as described in Section 7.7.3d), (pg162).

e) Stress and pain: moderated mediation

The mediation of the stress pain relationship by social support was not conditional on trauma status and sex. Social support does not buffer the effects of stress differently for males and females, whether or not they experienced a trauma. "Social support reduces distress directly, regardless of whether undesirable events have been suffered" (Thoits, 1982, pg473).

10.5.4 Strengths of the study

This study differed from previous research regarding physical trauma, stress and pain in its design and sampling frame, and its assessment of pain and adult physical trauma. These factors are discussed in turn.

a) Study design

As detailed in Section 2.2.3c, pg32, the majority of previous physical trauma and pain research has focused on exploring a direct association between widespread pain and self-reported trauma and the populations studied have tended to be female patients. Few studies have considered the role of psychological stress, used multivariable analysis, considered any mediator or moderator analysis or employed testable

theoretical models. This study involved the testing of a diathesis stress model, using structural equation modelling. This allowed the simultaneous assessment of multiple factors. The direct association between psychological stress and the number of pain sites was assessed, followed by an examination of the moderation of this relationship by adult physical trauma and sex. The mediation by social support and personal control was then examined to assess the pathway from psychological stress to pain. The analysis was performed for a population sample of both males and females.

b) Sampling frame

The NorStOP study used a community sample of adults aged 50 years and over obtained using General Practice registers. The population sample was drawn from a broad range of deprivation ratings making the sample representative of the general UK population of this age group and therefore the results of the study generalisable.

c) Number of pain sites

As described in Section 7.7.4c), (pg170), the use of a count of the number of pain sites has advantages over the use of a dichotomised outcome measure. The count of the number of pain sites provides a finer level of detail for the assessment of risk factors and may also provide an indication of an individual's level of functional impairment (Kamaleri et al, 2008a).

d) Assessment of adult physical trauma

Previous research has focused on the retrospective self-report of a previous trauma prior to the development of widespread pain (Broderick & Ross, 2005; Pamuk et al, 2009; ter Borg et al, 1999). This can result in potential recall bias as described in Section 7.7.3b) (pg156). Other studies have followed individuals who have experienced particular types of traumatic events. This provides an objective measure of a traumatic event; however this design often fails to include an appropriate control group. For example, in the studies by Tishler et al (2006; 2011) and Buskila et al (1997) individuals

who had experienced fractures were compared to individuals experiencing neck or spinal injuries. An appropriate control group would include individuals who had not experienced a traumatic event, allowing for a comparison with the natural course of the development of widespread pain. The current study combined the most effective aspects of both of these study designs by using an objective measure of trauma in a community sample, and also allowing for a comparison with individuals without a trauma history.

10.5.5 Limitations of the study

A number of limitations within the current study have been identified. These include the assessment of widespread pain, as described in Section 7.7.5b), the study design and the assessment of psychological stress and adult trauma.

a) Study design

One limitation of this study was it use of secondary data. This restricted the factors available for inclusion in the analysis. A number of biological, psychological and social factors have been associated with the development and persistence of widespread pain as described in Section 2.5.2. Further details of the additional factors of interest are provided in Section 11.9. In addition, the NorStOP study was not specifically designed for moderation and mediation analysis. As described above, in order for an optimum assessment of mediation, the mediator variables are ideally measured after the predictors, but before the outcome variables. The lead time of three years between baseline data collection and follow up may also have reduced the predictive ability of psychological stress. Participants may have changed both pain and psychological stress status more than once within this time period.

b) Psychological stress

This study combined the effects of anxiety, depression and sleep problems in a latent variable. The *psychological stress* latent variables did not fit the NorStOP data as well as the GPSS data. This may be due to the older age of participants or the substitution of

sleep problems for somatisation and life events. The use of only three observed variables meant that the latent variable was only just identified (as described in Section 4.6.1). Future research should consider how to conceptualise and assess psychological stress. This may involve the inclusion of additional measures, as discussed in Section 11.9.1).

c) The assessment of adult trauma

Although the use of medical records can be considered as an objective assessment of physical trauma, problems can occur in the reporting, recording and interpretation of such events. The primary purpose of medical records is for patient care (Jansen et al, 2005). Information is supplied by the patient to the GP, who records the details in the records using a read code. This process relies on the patient providing complete and accurate details to the GP, the correct interpretation of the details by the GP and the availability and appropriate use of read codes. Thus an element of subjectivity is added. For example, GPs may take different coding approaches, recording in relation to the cause of an injury e.g. RTA or its consequence, e.g. a fracture. Also, if the patient presents with multiple problems, not all may be recorded. The cause may only be coded if there is no code for the consequence or if there is no specific injury (Professor Christian Mallen, personal communication 27/4/12). "Medical record reviews are plagued by problems regarding the reliability and validity of the record itself and the data extracted from it" (Rask et al, 2010, pg350). However, the quality of general practice clinical data can be improved with training and regular auditing (Porcheret et al, 2004).

A further potential issue with the use of medical records was the identification of read codes that represent traumatic events. Read codes themselves do not provide any information regarding the severity or impact of the event. The misclassification of a read code may have resulted in individuals being allocated to an incorrect group. For example, the inclusion of inappropriate, non-trauma related codes may have resulted in individuals being incorrectly classified as experiencing trauma when they did not, thus

weakening and diluting the moderation effect. In order to mitigate this potential for error, read codes were classified in consultation with three practicing GPs. Only those read codes deemed to be traumatic by all three GPs were classified as such. A list of included read codes was presented in Table 8.2, whilst excluded read codes are listed in Appendix 5.

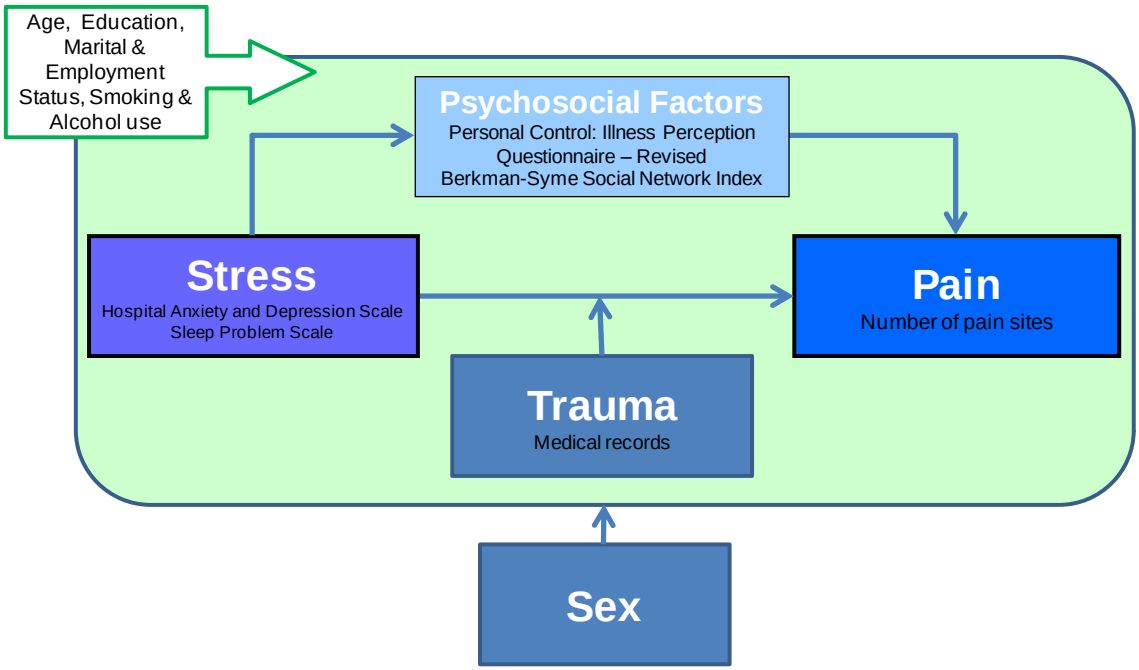
The use of medical records also precludes any traumas for which the individuals did not consult their GP. Although it is unlikely that the patient would not have any contact with their GP regarding surgeries, fractures and burns there is the possibility that a GP was not consulted following a RTA. However, the aim of the medical record review was to identify physically traumatic events. If a RTA did not require medical attention then it would not meet the inclusion criteria for this research.

And finally, no assessment was made of any treatments that the participants may have received prior to the baseline survey or between baseline and follow up. The fact that the physical trauma was recorded on the patients' medical records would indicate the receipt of some form of treatment, which may have reduced the impact of the trauma and stress and thus the risk of the development of widespread pain.

10.5.6 Key findings and implications for the trauma diathesis stress model of widespread pain

This section revisits the trauma diathesis stress model of widespread pain presented in Section 2.5, pg50 (Figure 10.4). The results from the NorStOP analysis provide contributions to the knowledge in the trauma, stress and pain field in addition to those of the GPSS study highlighted in Section 7.7.6 (pg174). The trauma diathesis stress model has been refined to reflect the key findings from the NorStOP analysis (Figure 10.5).

Figure 10.4 Proposed adult physical trauma diathesis stress model of widespread pain



Source: original

1) Adult physical trauma does not moderate the stress pain relationship

Overall, the results suggest that traumatic experiences such as surgeries, fractures, RTAs and burns occurring in adulthood do not increase an individual's susceptibility to widespread pain when they become stressed in those aged 50 years and over.

2) Social support mediates the stress pain relationship

The identification of the mediating effect of social support was also a major contribution of the NorStOP study. Previous research has shown that social support reduces the risk of the development and persistence of widespread pain (Bergman et al, 2002; Thomten et al, 2011). However, the results of this research provided evidence of a mediation effect of social support, identifying one of the mechanisms by which psychological stress can lead to widespread pain.

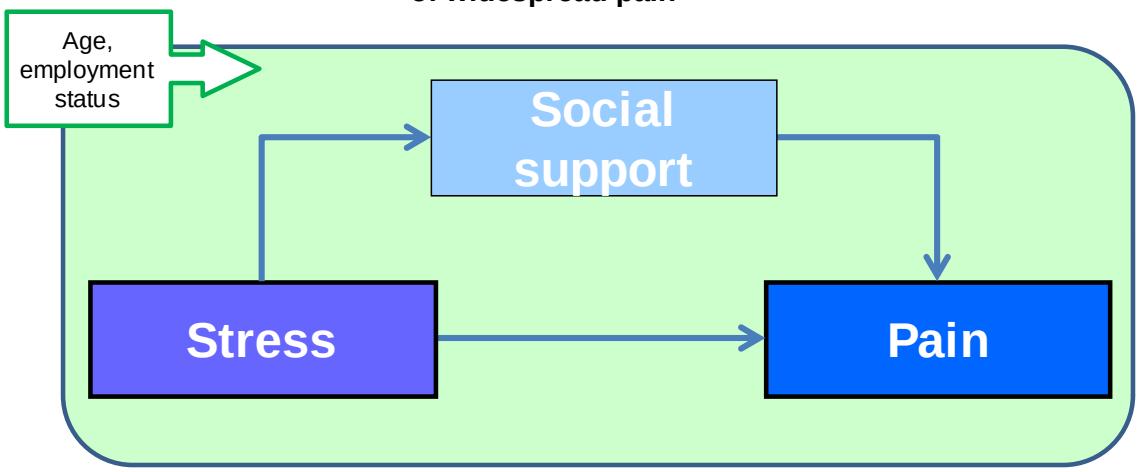
3) The relationships were not different in males and females

There was a significant difference in the number of pain sites between males and females in the bivariate analysis (Table 10.1). However, there was no difference

between males and females in the strength of the stress pain relationship, the moderation by adult physical trauma or the mediation effect of social support.

In light of the findings from the current study, the trauma diathesis stress model of widespread pain has been refined (Figure 10.5). The adapted model shows a direct association between stress and pain, mediated by social support, but without any moderation effect of trauma or sex.

Figure 10.5 Adapted adult physical trauma diathesis stress model of widespread pain



Source: original

10.6 Chapter summary

This chapter presented the results of the analysis of the trauma diathesis stress model of widespread pain. An increase in psychological stress was associated with an increase in the number of pain sites. This stress pain relationship was mediated by social support, but this mediation effect was not moderated by adult trauma and sex. The aim of this study was to identify whether adult trauma increased susceptibility to widespread pain in individuals who experience psychological stress. The results of the study suggest that adult trauma does not increase susceptibility. Potential explanations for the findings were discussed along with an examination of the strengths and limitations of the research, the implications of the findings for the trauma diathesis stress model and the contribution this study has made to the trauma, stress and pain field. The implications of the findings for

the treatment of widespread pain and the recommendations for future research are described in Chapter 11.

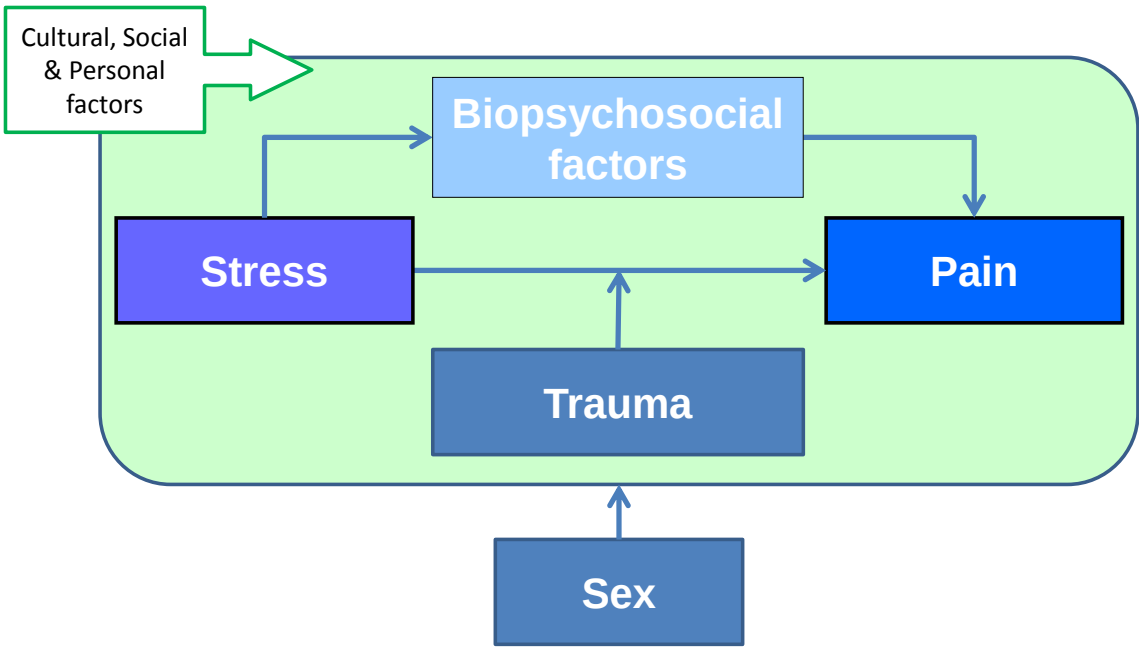
To summarise, the key findings from the NorStOP analysis were that the stress pain relationship was mediated by perceived social support, but was not moderated by adult physical trauma or sex.

Chapter 11 Discussion

11.1 Chapter overview

This chapter reviews and compares the findings from the GPSS and NorStOP studies with reference to the trauma diathesis stress model of widespread pain (Figure 11.1). Consideration is then given to the implications of the findings for Schnurr and Green's (2004a) trauma exposure and physical health model and for current treatment of widespread pain. This chapter will conclude with recommendations for future research.

Figure 11.1 Trauma diathesis stress model of widespread pain



Source: original

11.2 Psychological stress and widespread pain

The results of the GPSS and NorStOP analyses provide further evidence of the important role of psychological stress in the development and persistence of widespread pain. Whilst the GPSS analysis demonstrated the relationship in a community sample aged between 25 and 65 years (cross-sectional median 47 years; prospective median 50 years), the NorStOP analysis confirmed the relationship in an older community sample, aged 50 to 90 years of age (median 64 years).

11.3 Childhood abuse, but not adult physical trauma, moderates the stress pain relationship

The aim of the studies presented in this thesis was to ascertain whether individuals with a history of trauma have an increased susceptibility to widespread pain when they experience psychological stress. The findings suggest that such susceptibility was increased by childhood abuse, but not by surgeries, fractures, RTAs or burns in adulthood.

The traumatic experiences examined differed in the age at which they occurred and in type. The GPSS analysis examined interpersonal trauma occurring during childhood, whilst the NorStOP analysis examined physical trauma occurring during adulthood. It is possible that trauma experienced during the development of the nervous system and particularly the stress and pain processing systems, (i.e. during childhood) would have a greater impact on susceptibility than trauma experienced once these systems have matured (i.e. during adulthood). On the other hand, it may be that physical trauma is less damaging than interpersonal trauma. It is possible that the psychological impact of trauma has more of an influence on the development and persistence of widespread pain, than the timing or type of event. Previous research suggests that the psychological impact of trauma may be higher as the result of early life compared to later life trauma (Ogle et al, 2013; Maschi et al, 2011; Boals et al, 2012), and interpersonal compared to non-interpersonal trauma (Ogle et al, 2013). This supports the findings from the current studies. Surgeries, fractures, RTAs and burns, whilst being physically traumatic may not necessarily be psychologically traumatic. It is also possible that childhood abuse is not always psychologically traumatic (as alluded to in Section 7.7.5) and this may account for the differences in the findings between the cross-sectional and prospective analysis.

11.4 Sex moderates the effects of childhood abuse, but not adult physical trauma

There was no significant difference between males and females in the strength of the stress pain relationship in either the GPSS or NorStOP studies. In the GPSS analysis, the mediation of the stress pain relationship by adult attachment style was moderated by childhood abuse and sex. This may be suggestive of differences between the sexes in the type of childhood abuse experienced and the way abuse is interpreted and dealt with, as discussed in Section 2.5.3b (pg68). In the NorStOP analysis, however, the mediation by social support was not conditional upon trauma status or sex, which suggests a more general effect. This could indicate that different widespread pain treatment strategies are required for males and females with a history of childhood abuse, but not for males and females who have experienced a physical trauma.

11.5 Mediators of the psychological stress and widespread pain relationship

Mediation analysis was performed to identify the psychosocial mechanisms by which stress leads to pain. The stress pain relationship was not mediated by any of the psychological factors examined: dissociation, health anxiety, somatosensory amplification (GPSS) or personal control (NorStOP). The stress pain relationship was, however, mediated by the two social factors; adult attachment style (GPSS) and social support (NorStOP).

11.5.1 Adult attachment style

Adult attachment style was found to be a significant mediator of the stress pain relationship in both the cross-sectional and prospective GPSS analyses. Attachment style determines expectations and beliefs concerning social situations, and consequently how individuals respond to stressful situations (Bowlby, 2007). An insecure adult attachment style may result in detrimental alterations to the stress and pain processing systems, an increase in unhealthy behaviours and a decrease in the use of protective factors (Maunder & Hunter, 2001).

11.5.2 Social support

Social support was found to be a significant mediator of the stress pain relationship in the NorStOP analysis, but not in the GPSS analysis. This difference may be due to the age difference of the participants, or to the way in which social support was assessed. Patterns of social networks and requirements from social support change with age. For example, the number of peripheral contacts decreases, whilst more intimate relationships become more important (Carstensen, 1995). Thus as individuals age they become more selective in their relationships and social support becomes more strongly associated with life satisfaction (Li et al, 2011). It is possible that social support mediates the stress pain relationship only as individuals become older. Alternatively, in the GPSS survey social support was assessed using a single question "Do you have someone with whom to discuss personal problems or turn to in a time of crisis?" The NorStOP survey used the Berkman-Syme Social Network Index (BSNI), which is based on marital status, number of friends and relatives, the frequency of contact and also membership of social, community and religious groups. Therefore, the use of the BSNI allowed for a more sophisticated assessment of social support. Further research is required in order to ascertain whether this difference in the mediation of the stress pain relationship by social support was due to the age of the cohort or the use of the BSNI. High levels of social support may result in beneficial alterations to the stress and pain processing systems, a decrease in unhealthy behaviours and an increase in the use of protective factors (Ditzen et al, 2008; Warner et al, 2011).

Both adult attachment style and social support provide partial explanations of how stress leads to widespread pain. An insecure attachment style and a lack of social support have both been previously associated with reduced self-esteem. For example, both fearful and preoccupied attachment styles are associated with a negative view of the self (Bartholomew & Horowitz, 1991), whilst social exclusion can imply rejection or disapproval and thus can have a detrimental effect on self-esteem (Leary et al, 1995).

Furthermore, low self-esteem has been associated with increased PTSD symptoms in individuals with a history of childhood abuse (Muller et al, 2000) and has also been shown to be present in female FM patients (Johnson et al, 1997; Compan et al, 2011). This then may provide insight into the findings presented in this thesis, that self-esteem is a possible common factor for both attachment style and social support. Further work examining how attachment style, social support and self-esteem interact with widespread pain may be worthy of further consideration.

11.6 Generalisability of findings

In both the GPSS and NorStOP studies, the prevalence of childhood abuse, the incidence of adult physical trauma and the levels of pain, psychological stress, dissociation, health anxiety, somatosensory amplification, personal control, adult attachment and social support were broadly similar to the findings of previous general population studies involving participants with similar ages. This would suggest that the study population was representative of the general population. Psychological stress was shown to be robustly associated with widespread pain in cross-sectional and prospective analyses, in participants with a wide range of ages. The consistency of this association would suggest that it is highly likely to be generalisable to the general population.

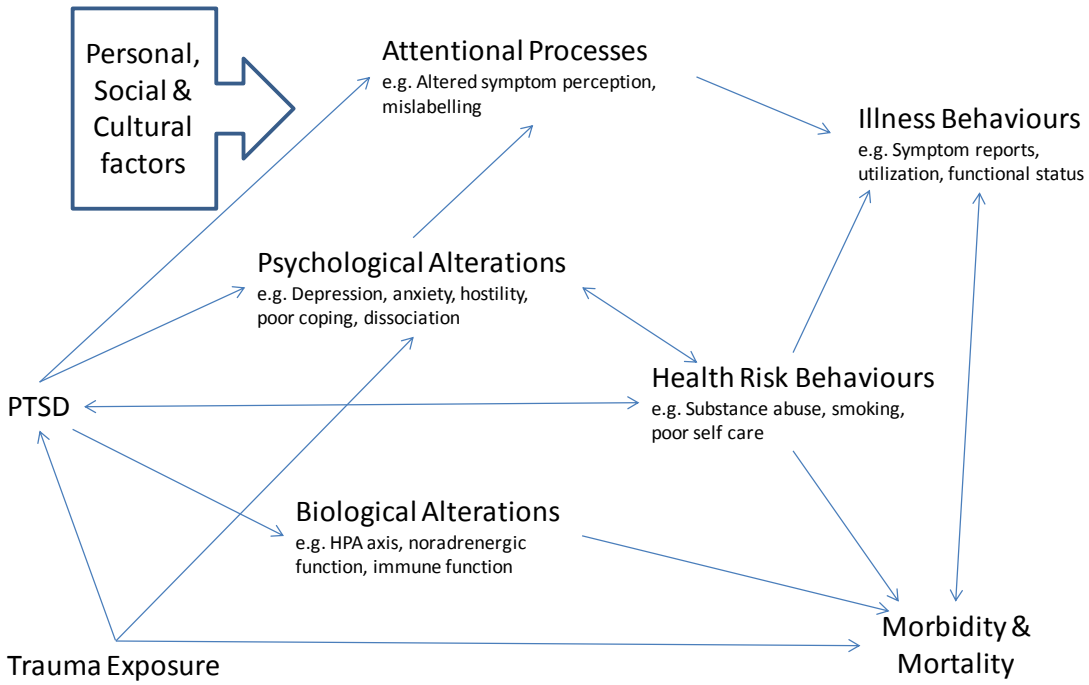
There was a difference between participants and non-participants in both the GPSS and NorStOP studies. Firstly, participants in both studies were more likely to be female and older than non-participants. These factors were accounted for in the analysis by controlling for age and moderation by sex. Secondly, the participants' levels of psychological stress were lower than non-participants in both studies. However, the differences were small (zero or one difference in medians) and the levels for participants were consistent with those of previous research. Finally, participants in the NorStOP study reported higher levels of personal control and social support than non-participants although, again, the levels for participants were consistent with previous research.

Overall, the similarity and consistency of the findings with previous research would suggest that the novel findings (mediation, moderation and moderated mediation) of this research are also independent of the study population and therefore would be generalisable to the general population.

11.7 The model of trauma exposure and physical health - revisited

The trauma diathesis stress model of widespread pain was developed from the model of trauma exposure and physical health as described in Section 2.4.2 (pg48) and Figure 11.2 (Schnurr & Green, 2004a). This model proposed that traumatic experiences lead to posttraumatic stress symptoms, which produce biological, psychological and attentional alterations. The resulting health risk and illness behaviours then lead to physical ill health.

Figure 11.2 A model of trauma exposure and physical health

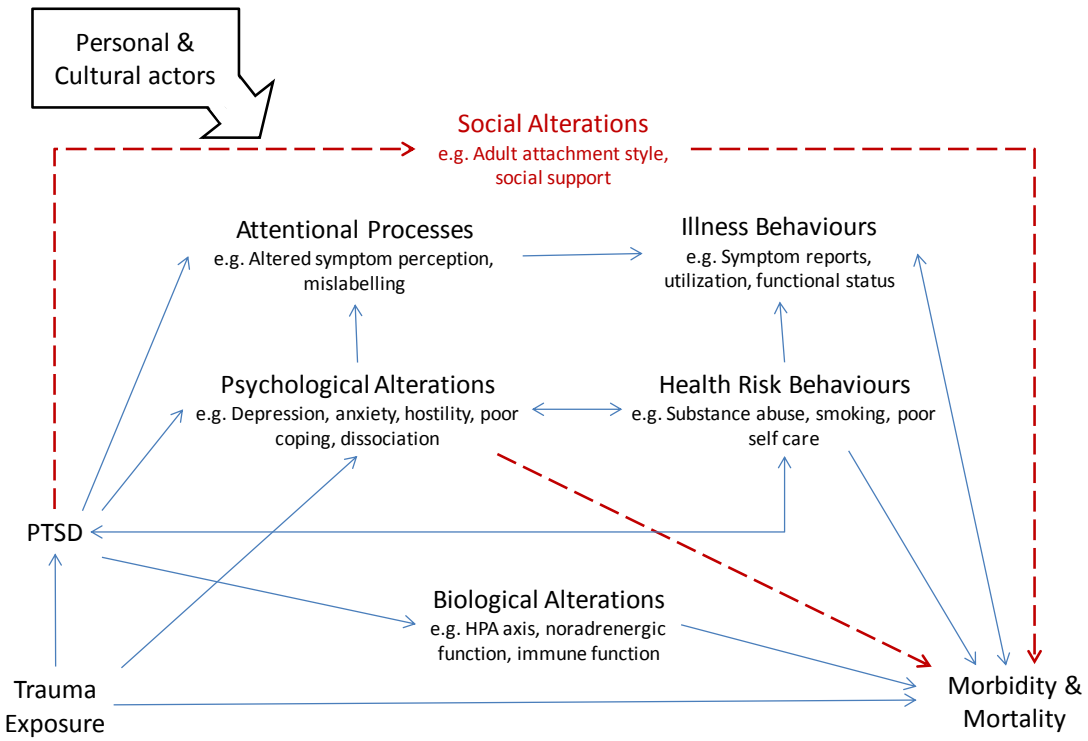


Source: Schnurr and Green (2004a)

The model of trauma exposure and physical health was not specifically tested, however the findings from the current studies partially concur with this model. Both the GPSS and NorStOP analyses found a significant direct association between psychological stress (including anxiety and depression) and widespread pain. This would suggest the

requirement to add a direct link either from PTSD or psychological alterations to morbidity. However, it is possible that anxiety and depression lead to widespread pain via health risk behaviours, the influences of which were not assessed in the current studies. Dissociation, health anxiety and personal control (psychological alterations) and somatosensory amplification (an attentional process) were not found to mediate the stress pain relationship. Again, however, their effect through illness and health risk behaviours was not specifically tested here. Adult attachment style (GPSS study) and social support (NorStOP study) were identified as significant mediators of the stress pain relationship. Although Schnurr and Green (2004a) acknowledge the influence of social, personal and cultural factors, perhaps adult attachment style and social support should be included as "social alterations" on the pathway from trauma exposure / PTSD to morbidity / mortality. In this way, social alterations would be given more presence, equal in parity to psychological and biological alterations (Figure 11.3).

Figure 11.3 Adapted model of trauma exposure and physical health



Source: adapted from Schnurr and Green (2004a)

11.8 Implications for treatment

As outlined in Section 2.6 (p72), current treatments for widespread pain result in only small to moderate symptom improvement, often of short duration (Nuesch et al, 2013). One of the reasons why such treatments are not successful is because widespread pain is the result of a complex interaction of factors. Individuals with widespread pain are therefore heterogeneous (Van Houdenhove & Luyten, 2008), suggesting that a stratified approach to treatment may be more successful. By exploring the moderators (in whom) and mediators (mechanisms) of the stress pain relationship, the trauma diathesis stress model of widespread pain has enabled the identification of susceptible individuals and also identified possible social processes that could be targeted in treatment. The relationship between psychological stress and widespread pain was significant in both the GPSS and NorStOP studies. It follows, therefore, that the existing treatments which target psychological stress, particularly anxiety, depression, somatisation, sleep problems and the response to recent life events would be beneficial not only for individuals with existing widespread pain conditions, but also as a prevention for its development.

Adult attachment style and social support were found to mediate the stress pain relationship. Whilst further research is required to clarify and confirm these findings, the results are suggestive of the role of these factors in the development of widespread pain. Current widespread pain treatments which target an individual's attachment style, such as CBT (Andersen, 2012), EMDR (Wesselmann et al, 2012) or group therapy (Marmarosh & Tasca, 2013) could therefore be beneficial. Support groups and group therapy have also been a beneficial source of social support to patients with widespread pain (van Uden-Kraan, 2008; Bremander et al, 2009). Patients report that support groups provide a sense of belonging, acceptance and solidarity. Patients learn from each other by sharing experiences, providing motivation and encouragement. Reported benefits also include being able to help others and taking pleasure from the achievement of others (Subramaniam et al, 1999; Matthias et al, 2014). Similarly, group CBT has enabled

patients to realise that it is acceptable to seek support and learn to recognise when it is needed (Bremander et al, 2009).

Researchers have suggested that childhood abuse and neglect should be screened for within primary care (Leserman et al 1998; Van Houdenhove et al, 2001; Green & Kimberling, 2004; Friedman et al, 1992; Sachs-Ericsson et al, 2009). Although NICE guidelines (NICE, 2013) are in place to identify abuse in children up to age 17 years, there are currently no plans to consider a screening policy for childhood abuse in adults (personal communication; Hugh Davis, UK National Screening Committee 25/02/2014). Screening for childhood abuse would only be beneficial if different treatments were required dependent upon abuse status. The finding from the GPSS analysis of a moderation effect on the stress pain relationship by childhood abuse suggests that a stratified approach should be used to effectively target treatment. Also the findings from the moderated mediation analysis suggest that there may be different mechanisms by which stress leads to pain dependent upon abuse status and sex. The trauma focused therapies identified in Section 2.6 (p72), may therefore be beneficial. These include trauma focused CBT, EMDR and psychodynamic psychotherapies. In addition, dialectical behaviour therapy (DBT) has been found to be effective for the treatment of PTSD and childhood abuse related symptoms (Steil et al, 2011; Bohus et al, 2013). DBT is an individual and group therapy based on CBT and Buddhist meditative practice. Treatment includes interpersonal skills training to improve stress tolerance and to facilitate acceptance and mindful awareness (Read, 2013).

“Ultimately stratified medicine will ensure that the right patient gets the right treatment at the right time” (MRC, 2014). The STarTBack approach to screening and stratifying treatment for individuals with low back pain is a good example (Hill et al, 2008). The STarTBack tool contains four questions concerning pain and disability and five psychosocial questions based on recognised prognostic factors. The tool enables GPs to identify low, medium and high risk low back pain patients. Treatment is then provided

according to this risk; low risk patients receive education and pharmacological treatment, medium risk patients receive physiotherapy, and CBT combined with physiotherapy is provided to the high risk group (Hill et al, 2008). This strategy has proved effective for the patient and also cost-effective for the treatment provider (Hill et al, 2011). However, in a recent survey, family physicians in Massachusetts, USA identified a number of barriers to screening for a history of abuse, including a lack of time and training and discomfort with asking. There was also a perception that there was little they could do to help such patients and a belief that a history of childhood abuse was not a medical problem (Weinreb et al, 2010). Prior to the introduction of screening, training will therefore be required for health care professions regarding the long term impact of childhood abuse, how to interact with patients disclosing abuse and how and to whom to refer disclosing patients (Schnurr & Green, 2004a).

The results of the studies reported in this thesis suggest that the stress pain relationship is moderated by childhood abuse, but not adult physical trauma and is mediated by adult attachment style and social support. These findings have implications for the treatment of widespread pain, suggesting that a stratified approach may be most appropriate. However, further research is required to clarify and build upon these findings.

11.9 Recommendations for future research

The research documented in this thesis focused on specific psychosocial mediators. In order to further understand the relationship between stress and pain, future research should examine alternative and / or supplementary mediators. Similarly, additional information relating to traumatic experiences may enable the more precise identification of susceptible individuals, whilst other potential susceptibility factors, such as genetics (Limer et al, 2008), deprivation (Khang et al, 2013), temperament and personality (Gatchel et al, 2007) could also be considered. Building on the findings from the studies

documented in this thesis, further research is required with regard to potential screening activities and stratified treatment provision. Each of these areas is discussed in turn.

11.9.1 Psychological stress

Assessing psychological stress using a combination of life threatening events, anxiety, depression, and somatisation (GPSS) was a better fit to the data than using anxiety, depression and sleep problems (NorStOP). As discussed in Section 2.3.1 (pg38), there are three approaches to assessing stress. The GPSS analysis included environmental and psychological aspects of stress. Future research could also include biological measures to assess allostatic load, such as cortisol and catecholamine levels and blood pressure (McBeth et al, 2007; McEwen, 1998). Two alternative prospective models were examined in the GPSS analysis. Although the model fit statistics were better for the controlling for baseline pain model, the pain as a stressor model still fit the data well. It would therefore be interesting to explore this latter model further, particularly as there was a trend for the relationship between the number of pain sites at baseline and follow up to vary with abuse status (see Section 7.7.3biii).

11.9.2 Mediators of the stress pain relationship

Widespread pain results from a complex interaction of multiple physiological, psychological and social factors (Clauw & Crofford, 2003). Future research should examine factors that have been associated with widespread pain, but were not examined in the current studies. These include (but are not limited to) alternative psychological factors, including self-efficacy, coping strategies (Smith et al, 2009) and catastrophising (Edwards et al, 2006). Furthermore, the GPSS and NorStOP studies examined the mediation effect of psychosocial factors individually, and yet it may be that such processes interact. To fully understand the relationship between stress and widespread pain it may be necessary to investigate how such factors work together over time. For example, future research is required to further clarify the pathways from stress to pain identified in the current research. With regard to adult attachment, does a fearful style

lead to prolonged activation of the stress system, increasing the risk of widespread pain? Similarly, does social support reduce the risk of the development of widespread pain by increasing levels of self-efficacy? However, the inclusion of further variables would necessitate a large sample size and may make interpretation of findings more complex. Ideally, prospective data would be collected from a large community population to enable further sub-groups / moderation analysis. Furthermore, multiple and frequent data collection points would enable the examination of chronology and potentially causality and a wide age range would be useful to aid the identification of any sensitive period for the development of susceptibility.

11.9.3 Moderators of the stress pain relationship

The GPSS and NorStOP studies examined the moderation effect of childhood interpersonal and adult physical trauma, respectively. Individuals with widespread pain also report the occurrence of adult interpersonal trauma, such as domestic violence and rape (Dutton et al, 2006; Balousek et al, 2007; Wuest et al, 2009; Hauser et al, 2012; McLean et al, 2012) more frequently than the general population. Research also suggests that physical trauma in childhood can have long term detrimental effects on the stress and pain processing systems (McBeth et al, 2001c, Wang et al, 2004; Mallen et al, 2006; Walker et al, 2009b; Slater et al, 2010). However, to date research has examined a direct association between these trauma types and widespread pain and the findings have not always been consistent (Hauser et al, 2011).

Although research suggests that different traumatic experiences lead to different short term and long term emotional responses (Amstadter & Vernon, 2008), the response to trauma is also dependent upon an individual's personality, prior experience, their perception of the event and also the reactions of others (Yehuda & DeLoux, 2007; O'Leary et al, 2010). Future studies should therefore include an assessment of the impact of the trauma. This could be achieved by the use of a structured clinical interview (Elhai et al, 2005) or questionnaires, such as the Post-traumatic Stress Symptoms Scale (Foa et

al, 1993), the Impact of Events Scale (Christianson & Marren, 2013; Horowitz, 1979), or the Centrality of Events Scale (Berntsen & Rubin, 2006). This would enable the identification of further sub-groups and the examination of the moderation effect of the psychological impact of trauma, in addition to the occurrence of such events.

In order to further clarify the role of trauma in the development and persistence of widespread pain, whether susceptibility is increased by childhood or adulthood, physical or interpersonal trauma, or the psychological impact of the trauma, future research examining the trauma diathesis stress model of widespread pain should examine the occurrence and impact of multiple trauma types occurring across the lifespan within the same population.

11.9.4 Further applications of the trauma diathesis stress model

Traumatic experiences and psychological stress have been implicated in the development of a number of psychological and physical health problems. It would be interesting to examine whether the trauma diathesis stress model could be applied to conditions other than widespread pain, for example, irritable bowel syndrome (Leserman & Drossman, 2007) chronic pelvic pain (Lampe et al, 2003), Alzheimer's disease (Burnes & Burnette, 2013) and schizophrenia (Read et al, 2005). It would also be interesting to examine why some traumatised individuals go on to develop physical problems, others develop psychiatric disorders and yet others experience post-traumatic growth (Merecz et al, 2012; Woodward & Joseph, 2003; Easton et al, 2013).

11.9.5 Screening and treatment

The findings from the GPSS study suggest that individuals who report childhood abuse and neglect have an increased susceptibility to widespread pain when they experience psychological stress. As stated above, further research is required to identify whether susceptibility to stress and widespread pain is increased by a particular trauma type (interpersonal or physical), trauma occurring at a specific developmental phase (childhood

or adulthood) or whether susceptibility is increased based on the response to the event (e.g. post-traumatic symptoms). Further research would then be required to develop or identify a reliable and valid screening tool and to identify the most appropriate time to screen for the trauma types identified or the trauma related reactions. Research is also essential to determine when such screening should take place. Screening routinely during any primary care visit, whilst allowing trauma related issues to potentially be addressed prior to the development of any psychological or physical ill health, would seriously increase the GPs workload. Screening at the first report of the experience of pain, may enable treatment to prevent the pain from becoming more widespread or chronic. Alternatively, enquiries about a history of trauma could be made when pain that is resistant to usual treatment has been identified. Further research is also required to identify the most appropriate and effective interventions for individuals with widespread pain based on the outcome of the screening. Furthermore, training in the use of tools and the patient's response to the screening must also be considered.

Psychological stress has been shown to play an important role in the development and maintenance of widespread pain. It would therefore be beneficial to investigate the benefits and practicalities of screening for psychological stress within primary care (Green & Kimberling, 2004). The UK National Screening Committee will be reviewing their screening policy with regard to depression this year (Public Health England, 2010), and screening for anxiety, somatisation, sleep problems and PTSD should also be considered in future research (Kimberling et al, 2006).

11.10 Conclusion

Widespread musculoskeletal pain, the most common form of chronic pain, is disabling and costly. "Chronic pain is a condition in its own right" (NHS Scotland, 2008, pg3) and can be considered a public health burden. The research presented in this thesis has contributed new knowledge regarding the aetiology and mechanisms of the development and persistence of widespread pain.

This thesis presented the trauma diathesis stress model of widespread pain, a theoretical model developed by the author. The model was tested in two population based prospective studies. This research identified childhood abuse and sex as potential susceptibility factors, and adult attachment style and social support as mechanisms via which psychological stress leads to widespread pain. Based on these findings and the work of Schnurr and Green (2004a) it is proposed that childhood abuse increases susceptibility by altering psychological, social and biological processes. The experience of subsequent psychological stress then leads to further psychological, social and biological alterations, which lead to the development of widespread pain.

By identifying individuals who were susceptible to widespread pain when stressed (moderators) and also pathways (mediators) by which psychological stress lead to widespread pain, these findings suggest that a stratified approach to the treatment of widespread pain should be investigated further.

Previous studies examining the development and persistence of widespread pain have considered the roles of psychological stress and trauma separately. In the studies presented in this thesis, the relationships between trauma, stress and pain were examined simultaneously using a diathesis stress model. This model may also be useful for examining the aetiology and mechanisms of other physical and mental health conditions.

This research has also provided indictors of further directions for research; to confirm these findings; to clarify further the mechanisms identified; to examine the potential benefits of screening for psychological stress and childhood interpersonal trauma and to inform treatment trials.

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Appendix 1 – Childhood interpersonal trauma and widespread pain review - Quality assessment

The assessment of the quality of studies and risk of bias within studies is essential, especially where findings differ, to guide understanding of those findings and differences and thus guide recommendations for future research and subsequently clinical care (Armijo-Olivo et al 2012). Two recent systematic reviews exploring trauma and pain (Paras et al, 2009; Hauser et al, 2011) used the Newcastle-Ottawa scale for assessment of study quality; however, this covers only cohort and case control studies. Although a recent systematic review identified 86 tools for the assessment of quality and risk of bias within cohort, case control and cross sectional studies (Sanderson et al 2007), Dr Paul Campbell and I found it necessary to develop our own tool as none of the existing check lists and scales allowed for studies examining cases as abused or CWP / FM or enabled a detailed assessment of the definition and measurement of both CWP / FM and childhood abuse and neglect (see below).

As recommended by Sanderson et al's (2007) review, our tool was created to clearly assess potential sources of bias using only "yes", "no" or "unclear" responses for simplicity and to avoid the need for subjective weightings of factors. The distinction between "no" and "unclear" reflects the difference between the quality of study methodology and the quality of study reporting. It is possible that some elements of methodology were not reported due to editorial decisions or space limitations within the publishing journal. The development of our tool was further informed by guidelines for study reporting (e.g. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE), von Elm et al, 2007), quality assessment (e.g. Effective Public Health Practice Project (EPHPP), Armijo-Olivo et al 2012) and identification of potential sources of bias (e.g. Hayden et al, 2006). As shown in below, the quality and risk of bias assessment tool, evaluated the methods for measuring trauma (childhood abuse and neglect) and pain (CWP / FM), selecting study participants and data analysis. Separate, additional evaluations were applied for studies using case control methodologies.

For the assessment of trauma, we considered whether the trauma was clearly defined; whether the age at which the trauma occurred was ascertained (e.g. childhood no points, before age 17 one point); whether the severity or frequency of trauma was ascertained and the reliability and validity of the measurement tool.

No preference was given to court documented abuse over retrospective self-report interviews or questionnaires, if reliability and validity information were provided for the latter, as each method has advantages and disadvantages (see Kendall-Tackett et al 2004). With regard to CWP / FM, the emphasis was again placed on the reliability and validity, such that a self-report of pain using reliable and valid measure was not seen as inferior to a diagnosis by the research team or clinic. However, an unconfirmed self-report of a diagnosis was considered as equal to a self-report measure without reliability and validity.

For study participation, scores were awarded if the sampling frame, recruitment, inclusion and exclusion criteria were described sufficiently to allow for replication; if demographic information was provided for the whole study population and if clear response rate and non-response analysis was provided. With regard to data analysis, scores were awarded to those studies with sufficient sample size for the statistical analysis performed and to those using multivariable analysis.

Additional quality / bias criteria were applied to case control studies. Those case control studies providing a clear description of the method of screening controls and where the same methods of screening cases and controls was used received higher quality scores.

Quality / bias was assessed independently by two authors (ADW, PC) and consensus was reached following discussions. Although the analysis was qualitative, a “yes” response was scored as one and a summary quality / bias score was assigned to each domain; trauma, pain, participation, data analysis (and case study, were appropriate) to aid comparisons.

Quality Assessment Tool

Trauma

Definition of Trauma	Trauma type clearly defined or questions provided	1	Y
	Not stated	0	N
	Unclear	0	U
Age of Trauma	Age of trauma clearly specified	1	Y
	Not stated	0	N
	Unclear	0	U
Severity of Trauma	Severity assessed or graded exposure (e.g. rarely, frequently etc)	1	Y
	Not Stated or yes / no response	0	N
	Unclear	0	U
Identification of Trauma	If severity assessed or graded exposure, clear statement of how dichotomised to yes / no response (e.g. any, or only severe)	1	Y
	Not Stated or yes / no response	0	N
	Unclear	0	U
Measurement of Trauma	Reference provided and / or validity and reliability information provided or court records	1	Y
	Not Stated	0	N
	Unclear	0	U

Pain

Measurement of Pain	Diagnosis (by research team or clinic), valid and reliable self-report measure (e.g. manikin)	1	Y
	Unconfirmed self-report of diagnosis, self-report measure with no reference, validity or reliability information or Not Stated	0	N
	Unclear	0	U

Participation

Sample Frame and Recruitment	Procedure adequately described	1	Y
	Inadequate or No description	0	N
	Unclear	0	U
Inclusion / Exclusion Criteria	Adequately described	1	Y
	Inadequate or No description	0	N
	Unclear	0	U
Baseline Population	Demographics described for whole population	1	Y
	Inadequate or No description	0	N
	Unclear	0	U
Response Rate	≥60% response rate	1	Y
	< 60% participation	0	N
	Unclear or not stated	0	U
Response / Non Response	Clear description of differences	1	Y
	Inadequate or No description	0	N
	Unclear	0	U

Data Analysis

Sample Size	Sufficient for chosen statistical analysis (> 5 * number of variables)	1	Y
	Insufficient or No description	0	N
	Unclear	0	U
Multivariate Analysis	Appropriate adjustments made	1	Y
	Univariate or adjustment not stated	0	N
	Unclear	0	U

Case Control Studies

Identification of Controls	Clear description of screening to define controls	1	Y
	Inadequate or No description	0	N
	Unclear	0	U
Definition of Controls	Same method of ascertainment as for cases	1	Y
	Different method or No description	0	N
	Unclear	0	U

Table A1.1 Summary of studies exploring and association between childhood abuse and neglect and widespread pain and FM

Date	Author	Country	Design	Population	Comparison Condition	Age per group (Y(SD))		%Female per group		Number per group		Trauma Type
2001	McBeth et al (c)	UK	Cross Sectional	Community	No / Other Pain		39 (30-48)		58		296	CA
2001	Van Houdenhove et al	Belgum	Case Control	Tertiary Care	MS / RA HC			CFS/FM MS/RA Cntl	38 (9.5) 40 (8.9) 38.3 (9.4)	CFS FM RA MS HC	54 41 26 26 95	CPA, CEA, CSA, SH, CEN
2005	Castro et al	Guatemala	Case Control	Tertiary Healthy controls	RA STRD HC			FM RA STRD HC	44.5 45.5 41.0 44.5	FM RA STRD HC	58 74 55 187	CPA, CEA, CSA
2009	Ruiz-Perez et al	Spain	Case Control	Tertiary Care	ENT	FM ENT	47.76 (7.95) 40.76 (23.36)		100	FM ENT	287 287	CPA, CEA, CSA
2000	Anderberg et al	Sweden	Case Control	Tertiary Employees	HC	FM	48.6 (7.5)		100	FM HC	40 38	CE/PA, CSA, CN
2005	Ciccone et al	USA	Case Control	Community	HC	FM Cntl[1]	50.5 (10.6)		100	FM HC	52 53	CPA, CSA
1999	Goldberg et al	USA	Case Control	Tertiary Care	MP FP OCP	FM MP FP OCP	43.94 39.61 38.68 41.48	FM MP FP OCP	94 76 86 48	FM MP FP OCP	17 21 22 31	CPA, CSA, CEA
1995	Boisset-Pioro et al	Canada	Case Control	Tertiary Care	RD	FM RD	49.3 (20-70) 51.2 (19-70)		100	FM RD	83 161	CPA, CSA
1998	Carpenter et al	USA	Case Control	Tertiary Care	RA		51.2		100	FM RA	105 44	CPA, CSA
2011	Fuller-Thompson et al	Canada	Cross Sectional	Community	No FM		18-80		100		7070	CPA
2010	Haviland et al	USA	Cross Sectional	Community	HC		61.0 (13.5)		67		9644	CEA/N, CPA

Table A1.1 Summary of studies exploring and association between childhood abuse and neglect and widespread pain and FM cont

Date	Author	Country	Design	Population	Comparison Condition	Age per group (Y(SD))		%Female per group		Number per group		Trauma Type
2003	Imbierowicz et al	Germany	Case Control	Tertiary Care	SOM MEP	FM SOM MEP	42.3 (9.6) 41.9 (11) 41.6 (12.1)	FM SOM MEP	74 70 36	FM SOM MEP	38 71 44	CPA, CSA
2010	Smith et al	USA	Case Control	Tertiary Advertisements	HC		48.44 (6.91)		100	FM HC	41 44	CPA, CEA, CSA
1997	Walker et al	USA	Case Control	Tertiary Care	RA		not provided		100	FM RA	32 28	CPA, CEA, CSA, CN
2000	Finestone et al	Canada	Cross Sectional	Psychiatric Patients & Nurses	PP Nurses[2]		34.95 (9.07)		100	CSA PP Nurses	26 33 21	CSA

Key
CFS = Chronic Fatigue Syndrome; CWP = Chronic Widespread Pain; ENT = Ear, Nose and Throat patients without pain; FM = Fibromyalgia; FP = Facial Pain; HC = Healthy controls; MEP = Medically explained pain; MS = Multiple Sclerosis; MP = Myofascial Pain; OCP = Other Chronic Pain; PP = Psychiatric patients without CSA; RA = Rheumatoid Arthritis; RD = non FM rheumatic disorder; SOM = Somatoform pain disorder; STRD = Soft Tissue Rheumatic Disease; CPA = Childhood Physical Abuse; CSA = Childhood Sexual Abuse; CEA = Childhood emotional abuse; CN = Childhood Neglect; CEN = Childhood Emotional Neglect; CA = Childhood Abuse; CEA/N = combined Childhood Emotional Abuse and Neglect; SH = Sexual Harrasment - no contact
Note - 1 Healthy controls age matched; 2 Nurses without CSA

Table A1.2 Quality assessment of studies examining the association between childhood abuse and widespread pain

Year	Name	Trauma						Pain		Participation						Data Analysis			Case Control			Total
		Def	Age	Sev	Id	Meas	Total	MeaP	Total	Sam	InEx	Bas	Res	RnR	Total	Size	Mult	Total	Id	Defc	Total	
2001	McBeth et al (c)	n	y	u	u	y	**2**	y	**1**	y	y	y	y	y	**5**	y	y	**2**				***10***
2001	Van Houdenhove et al	y	y	y	y	y	**5**	y	**1**	y	n	y	n	n	**2**	y	n	**1**	n	n	**0**	***9***
	Total						***7***		***2***						***7***			***3***			*0*	***19***
2005	Castro et al	y	y	n	n	y	**3**	y	**1**	n	n	y	n	n	**1**	y	n	**1**	n	n	**0**	***6***
2009	Ruiz-Perez et al	n	n	y	y	y	**3**	y	**1**	y	y	y	n	n	**3**	y	n	**1**	y	y	**2**	***10***
	Total						***6***		***2***						***4***			***2***			*2*	***16***

Def = definition of trauma; Age = age of trauma; Sev = severity of trauma; Id = identification of trauma; Meas = measurement of trauma; MeaP = measurement of pain; Sample = sample frame and recruitment; InEx = inclusion / exclusion criteria; Bas = baseline population; Res = response rate; RnR = response / non response; Size = sample size; Multi = multivariable analysis; Id = identification of controls; Defc = definition of controls.

Table A1.3 Quality assessment of studies examining the association between childhood physical abuse and widespread pain / FM

Year	Name	Trauma						Pain		Participation						Data Analysis			Case Control			Total
		Def	Age	Sev	Id	Meas	Total	MeaP	Total	Sam	InEx	Bas	Res	RnR	Total	Size	Mult	Total	Id	Defc	Total	
2005	Ciccone et al	y	n	y	y	y	***4***	y	***1***	y	y	y	n	y	***4***	y	y	***2***	y	y	***2***	***13***
1999	Goldberg et al	y	y	n	n	y	***3***	y	***1***	y	y	y	y	y	***5***	y	y	***2***	y	y	***2***	***13***
2009	Ruiz-Perez et al	n	n	y	y	y	***3***	y	***1***	y	y	y	n	n	***3***	y	n	***1***	y	y	***2***	***10***
	Total						***7***		***2***						***9***			***4***			***4***	***26***
1995	Boisset-Pioro et al	y	y	y	n	y	***4***	y	***1***	y	y	y	u	u	***3***	y	n	***1***	y	y	***2***	***11***
1998	Carpenter et al	y	y	n	y	n	***3***	y	***1***	y	n	y	n	n	***2***	y	n	***1***	y	y	***2***	***9***
2011	Fuller-Thomson et al	n	n	n	n	n	***0***	n	***0***	y	n	y	y	n	***3***	y	y	***2***			***0***	***5***
2010	Haviland et al	y	n	n	n	y	***2***	n	***0***	y	y	y	n	n	***3***	y	y	***2***			***0***	***7***
2003	Imbierowicz et al	u	u	u	n	y	***1***	y	***1***	n	n	y	n	n	***1***	y	n	***1***	y	y	***2***	***6***
2010	Smith et al	n	n	n	n	y	***1***	y	***1***	n	y	y	n	n	***2***	y	n	***1***	y	y	***2***	***7***
1997	Walker et al	n	n	y	n	y	***2***	y	***1***	y	n	n	n	n	***1***	y	n	***1***	n	y	***1***	***6***
	Total						***13***		***5***						***15***			***9***			***9***	***51***

Def = definition of trauma; Age = age of trauma; Sev = severity of trauma; Id = identification of trauma; Meas = measurement of trauma; MeaP = measurement of pain; Sample = sample frame and recruitment; InEx = inclusion / exclusion criteria; Bas = baseline population; Res = response rate; RnR = response / non response; Size = sample size; Multi = multivariable analysis; Id = identification of controls; Defc = definition of controls.

Table A1.4 Quality assessment of studies examining the association between childhood sexual abuse and widespread pain / FM

Year	Name	Trauma						Pain		Participation						Data Analysis			Case Control			Total
		Def	Age	Sev	Id	Meas	Total	MeaP	Total	Sam	InEx	Bas	Res	RnR	Total	Size	Mult	Total	Id	Defc	Total	
2000	Anderberg et al	u	u	u	u	u	***0***	y	***1***	y	y	n	u	n	***2***	n	n	***0***	n	y	***1***	***4***
2005	Ciccone et al	y	n	y	y	y	***4***	y	***1***	y	y	y	n	y	***4***	y	y	***2***	y	y	***2***	***13***
1999	Goldberg et al	y	y	n	n	y	***3***	y	***1***	y	y	y	y	y	***5***	y	y	***2***	y	y	***2***	***13***
2009	Ruiz-Perez et al	n	n	y	y	y	***3***	y	***1***	y	y	y	n	n	***3***	y	n	***1***	y	y	***2***	***10***
	Total						***10***		***4***						***14***			***5***			***7***	***40***
1995	Boisset-Pioro et al	y	y	y	u	y	***4***	y	***1***	y	y	y	u	u	***3***	y	n	***1***	y	y	***0***	***9***
1998	Carpenter et al	y	y	n	n	y	***3***	y	***1***	y	n	y	n	n	***2***	y	n	***1***	y	y	***2***	***9***
2000	Finestone et al	y	y	n	n	y	***3***	y	***1***	y	y	y	y	n	***4***	y	n	***1***			***0***	***9***
2003	Imbierowicz et al	u	u	u	n	y	***1***	y	***1***	n	n	y	n	n	***1***	y	n	***1***	y	y	***2***	***6***
2010	Smith et al	n	n	n	n	y	***1***	y	***1***	n	y	y	n	n	***2***	y	n	***1***	y	y	***2***	***7***
1997	Walker et al	n	n	y	n	y	***2***	y	***1***	y	n	n	n	n	***1***	y	n	***1***	n	y	***1***	***6***
	Total						***14***		***6***						***13***			***6***			***7***	***46***

Def = definition of trauma; Age = age of trauma; Sev = severity of trauma; Id = identification of trauma; Meas = measurement of trauma; MeaP = measurement of pain; Sample = sample frame and recruitment; InEx = inclusion / exclusion criteria; Bas = baseline population; Res = response rate; RnR = response / non response; Size = sample size; Multi = multivariable analysis; Id = identification of controls; Defc = definition of controls.

Table A1.5 Quality assessment of studies examining the association between childhood emotional abuse and widespread pain / FM

Year	Name	Trauma						Pain		Participation						Data Analysis			Case Control			
		Def	Age	Sev	Id	Meas	Total	MeaP	Total	Sam	InEx	Bas	Res	RnR	Total	Size	Mult	Total	Id	Defc	Total	Total
1999	Goldberg et al	y	y	n	n	y	***3***	y	***1***	y	y	y	y	y	***5***	y	y	***2***	y	y	***2***	***13***
2009	Ruiz-Perez et al	n	n	y	y	y	***3***	y	***1***	y	y	y	n	n	***3***	y	n	***1***	y	y	***2***	***10***
	Total						***6***		***2***						***8***			***3***			***4***	***23***
2010	Smith et al	n	n	n	n	y	***1***	y	***1***	n	y	y	u	n	***2***	y	n	***1***	y	y	***2***	***7***
1997	Walker et al	n	n	n	n	y	***1***	y	***1***	y	n	n	n	n	***1***	y	n	***1***	n	y	***1***	***5***
	Total						***2***		***2***						***3***			***2***			*3*	***12***

Def = definition of trauma; Age = age of trauma; Sev = severity of trauma; Id = identification of trauma; Meas = measurement of trauma; MeaP = measurement of pain; Sample = sample frame and recruitment; InEx = inclusion / exclusion criteria; Bas = baseline population; Res = response rate; RnR = response / non response; Size = sample size; Multi = multivariable analysis; Id = identification of controls; Defc = definition of controls.

Table A1.6 Quality assessment of studies examining the association between childhood neglect and widespread pain / FM

Year	Name	Trauma						Pain		Participation						Data Analysis			Case Control			
		Def	Age	Sev	Id	Meas	Total	MeaP	Total	Sam	InEx	Bas	Res	RnR	Total	Size	Mult	Total	Id	Defc	Total	Total
2000	Anderberg et al	u	u	u	u	u	***0***	y	***1***	y	y	n	u	n	***2***	n	n	***0***	n	y	***1***	***4***
2003	Imbierowicz et al	u	u	u	n	y	***1***	y	***1***	n	n	y	n	n	***1***	y	n	***1***	y	y	***2***	***6***
1997	Walker et al	n	n	y	n	y	***2***	y	***1***	y	n	n	n	n	***1***	y	n	***1***	n	y	***1***	***6***
	total						***3***		***2***						***2***			***2***			***3***	***12***

Def = definition of trauma; Age = age of trauma; Sev = severity of trauma; Id = identification of trauma; Meas = measurement of trauma; MeaP = measurement of pain; Sample = sample frame and recruitment; InEx = inclusion / exclusion criteria; Bas = baseline population; Res = response rate; RnR = response / non response; Size = sample size; Multi = multivariable analysis; Id = identification of controls; Defc = definition of controls.

Appendix 2 – The General Practice Symptom Survey questionnaire

Demographic Information

Firstly, we would like to gather some background details:

A1 What is your date of birth? ☐☐ ☐☐ ☐☐☐☐

A2 Are you (please tick) Male ☐ Female ☐

A3 Are you (please tick)

Single	☐	Divorced	☐
Married / cohabiting	☐	Widowed	☐
Separated	☐		

A5 Are you (please tick one only)

Working full time	☐	Not working because of ill health / disability	☐
Working part time	☐	Student	☐
Working full time in the home	☐	Semi-retired	☐
Unemployed but seeking work	☐	Retired	☐

A8 Please indicate your highest educational or training qualification (please tick)

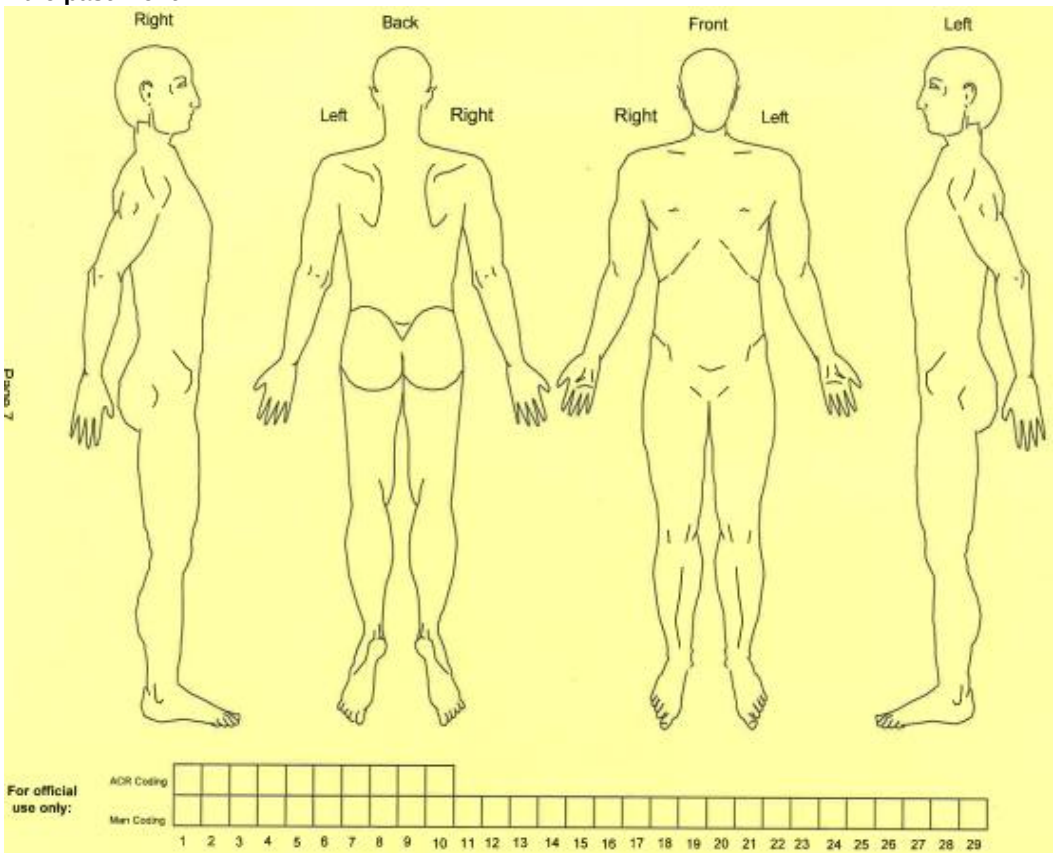
Post graduate qualification	☐
University graduate	☐
Educated to A levels / NVQ / BTEC / HND / OND	☐
Left education during secondary school	☐
Educated to O-levels or GCSEs	☐

Pain

We are now going to ask you some questions about pain.

C1 During the **past month** have you had any ache or pain which lasted for one day or longer? (please tick) Yes ☐ No ☐

C4 Please **shade** any area on the diagrams below where you feel, or have felt, these aches and pains over the **past month**:



Hospital Anxiety and Depression Scale

This section is concerned with feelings and emotions. Read each item and please a tick in the box opposite the reply which comes closest to how you have been feeling in the past week:

H1	I feel tense or 'wound up':	Most of the time	
		A lot of the time	
		Time to time, occasionally	
		Not at all	
H2	I still enjoy the things I used to enjoy:	Definitely as much	
		Not quite so much	
		Only a little	
		Hardly at all	
H3	I get a sort of frightened feeling as if something awful is about to happen:	Very definitely and quite badly	
		Yes, but not too badly	
		A little, but it doesn't worry me	
		Not at all	
H4	I can laugh and see the funny side of things:	As much as I always could	
		Not quite so much now	
		Definitely not so much now	
		Not at all	
H5	Worrying thoughts go through my mind:	A great deal of the time	
		A lot of the time	
		From time to time but not too often	
		Only occasionally	
H6	I feel cheerful:	Not at all	
		Not often	
		Sometimes	
		Most of the time	
H7	I can sit at ease and feel relaxed:	Definitely	
		Usually	
		Not often	
		Not at all	
H8	I feel as if I am slowed down:	Nearly all the time	
		Very often	
		Sometimes	
		Not at all	
H9	I get a sort of frightened feeling like 'butterflies in the stomach:	Not at all	
		Occasionally	
		Quite often	
		Very often	
H10	I have lost interest in my appearance:	Definitely	
		I don't take as much care as I should	
		I may not take quite as much care	
		I take just as much care as ever	
H11	I feel restless as if I have to be on the move:	Very much indeed	
		Quite a lot	
		Not very much	
		Not at all	
H12	I look forward with enjoyment to things:	As much as I ever did	
		Rather less that I used to	
		Definitely less than I used to	
		Hardly at all	
H13	I get sudden feelings of panic:	Very often indeed	
		Quite often	
		Not very often	
		Not at all	
H14	I can enjoy a good book or radio or TV programme:	Often	
		Sometimes	
		Not often	
		Very seldom	

Somatic Symptom Inventory

Below is a list of symptoms. For each one, please tick the box indicating how much it has bothered you over the past 6 months:

		Not at all	A little bit	Moderately	Quite a bit	A great deal
H15	Nausea or vomiting	☐	☐	☐	☐	☐
H16	Soreness in your muscles	☐	☐	☐	☐	☐
H17	Pain or cramps in your abdomen	☐	☐	☐	☐	☐
H18	Feeling faint or dizzy	☐	☐	☐	☐	☐
H19	Trouble with your vision	☐	☐	☐	☐	☐
H20	Your muscles twitching or jumping	☐	☐	☐	☐	☐
H21	Feeling fatigued, weak or tired all over	☐	☐	☐	☐	☐
H22	A fullness in your head or nose	☐	☐	☐	☐	☐
H23	Pain in your lower back	☐	☐	☐	☐	☐
H24	Constipation	☐	☐	☐	☐	☐
H25	Trouble catching your breath	☐	☐	☐	☐	☐
H26	Hot or cold spells	☐	☐	☐	☐	☐
H27	A ringing or buzzing in your ears	☐	☐	☐	☐	☐

List of Threatening Events

The following questions ask about recent events in your life: We would like to ask you some questions about personal situations that you may have encountered during the last six months. Although some of these things are personal and of a sensitive nature, it would help a great deal if you could answer all of them.

All answers will be kept strictly confidential. During the last 6 months, have you experienced any of the following:

L1	Serious illness or injury to yourself?	Yes	☐	No	☐
L2	Serious illness or injury to yourself?	Yes	☐	No	☐
L3	The death of a first-degree relative, including child or spouse?	Yes	☐	No	☐
L4	The death of a close family friend or a second degree relative?	Yes	☐	No	☐
L5	Separation due to marital difficulties?	Yes	☐	No	☐
L6	Broken off a steady relationship?	Yes	☐	No	☐
L7	A serious problem with a close friend, neighbour or relative?	Yes	☐	No	☐
L8	Been unemployed / seeking work for more than one month?	Yes	☐	No	☐
L9	Been sacked from your job?	Yes	☐	No	☐
L10	A major financial crisis?	Yes	☐	No	☐
L11	Problems with the Police or a Court appearance?	Yes	☐	No	☐
L12	Had something valuable lost or stolen?	Yes	☐	No	☐

Whitely Index

Below is a list of questions about your health. For each one, please tick the box indicating how much this is true for you:

		Not at all	A little bit	Moderately	Quite a bit	A great deal
I1	Do you worry a lot about your health?	☐	☐	☐	☐	☐
I2	Do you think there is something seriously wrong with you?	☐	☐	☐	☐	☐
I3	Is it hard for you to forget about yourself and think about all sorts of other things?	☐	☐	☐	☐	☐
I4	If you feel ill and someone tells you that you are looking better, do you become annoyed?	☐	☐	☐	☐	☐
I5	Do you find that you are often aware of various things happening in your body?	☐	☐	☐	☐	☐
I6	Are you bothered by many aches and pains?	☐	☐	☐	☐	☐
I7	Are you afraid of illness?	☐	☐	☐	☐	☐
I8	Do you worry about your health more than most people?	☐	☐	☐	☐	☐
I9	Do you get the feeling that people are not taking your illness seriously enough?	☐	☐	☐	☐	☐
I10	Is it hard for you to believe the doctor when he/she tells you there is nothing for you to worry about?	☐	☐	☐	☐	☐
I11	Do you often worry about the possibility that you have a serious illness?	☐	☐	☐	☐	☐
I12	If a disease is brought to your attention (through the radio, TV, newspapers, or someone you know), do you worry about getting it yourself?	☐	☐	☐	☐	☐
I13	Do you find that you are bothered by many different symptoms?	☐	☐	☐	☐	☐
I14	Do you often have the symptoms of very serious disease?	☐	☐	☐	☐	☐

Somatosensory Amplification Scale

Please indicate the degree to which each of the following statements are true of you in general. Place a tick by the response which best applies to you:

		Not at all	A little bit	Moderately	Quite a bit	A great deal
J1	When someone else coughs it makes me cough too					
J2	I can't stand smoke, smog, or other pollutants in the air					
J3	I am often aware of various things happening within my body					
J4	When I bruise myself, it stays noticeable for a long time					
J5	Sudden loud noises bother me					
J6	I can sometimes hear my own pulse or my heartbeat throbbing in my ear					
J7	I hate to be too hot or too cold					
J8	I am quick to sense the hunger contractions in my stomach					
J9	Even something minor, like an insect bite or splinter, really bothers me					
J10	I can't stand pain					

Dissociative Experiences Scale – Taxon

The following 8 questions consist of experiences that you may have had in your daily life. We are interested in how often you have these experiences. It is important, however, that your answers show how often these experiences happen to you when you are not under the influence of alcohol or drugs.
Please determine to what degree the stated experience applies to you, and circle a number to show what percentage of the time you have that experience:

M1 Some people have experience of finding themselves in a place and having no idea how they got there.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M2 Some people are told that they sometimes do not recognise friends or family members.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M3 Some people sometimes have the experience of feeling as though they are standing next to themselves or watching themselves so something and they actually see themselves as if they were looking at another person.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M4 Some people have the experience of finding new things among their belongings that they do not remember buying.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M5 Some people have the experience of feeling that their bosy does not seem to belong to them.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M6 Some people sometimes find that when they are alone they talk out loud to themselves.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M7 Some people find that in one situation they may act so differently compared with another situation that they feel almost as if they were two different people.

0	10	20	30	40	50	60	70	80	90	100

Never Always

M8 Some people sometimes find that they hear voices inside their head that tell them to do things or comment on things that they are doing.

0	10	20	30	40	50	60	70	80	90	100

Never Always

Social Support

P1 Do you have someone with whom you can discuss personal problems or turn to in a time of crisis? Yes ☐ No ☐

Relationship Questionnaire

Please circle a number on the scale that most closely applies to you:

Q1 It is easy for me to become emotionally close to others. I am comfortable depending on them and having them depend on me. I don't worry about being alone or having others not accept me.

1	2	3	4	5	6	7

Not at all like me — Somewhat like me — Very much like me

Q2 I am uncomfortable getting close to others. I want emotional close relationships, but I find it difficult to trust others completely, or to depend on them. I worry that I will be hurt if I allow myself to become too close to others.

1	2	3	4	5	6	7

Not at all like me — Somewhat like me — Very much like me

Q3 I want to be completely intimate with others, but I often find that others are reluctant to get as close as I would like. I am uncomfortable being without close relationships, but I sometimes worry that others don't value me as much as I value them.

1	2	3	4	5	6	7

Not at all like me — Somewhat like me — Very much like me

Q4 I am comfortable without close emotional relationships. It is very important to be to feel independent and self-sufficient, and I prefer not to depend on others or have others depend on me.

1	2	3	4	5	6	7

Not at all like me — Somewhat like me — Very much like me

Childhood physical and sexual abuse questionnaire:

We know that many people may have violent and / or unwanted sexual experiences as children. We would like you to help us understand these experiences by answering some questions. For each question, please tick one box to show whether you have had any such experiences.

All answers will be kept strictly confidential

When you were a child (16 or under), did an older person do the following

		Never	Seldom	Occasionally	Often
01	Hit, kicked or beat you				
02	Seriously threaten your life				
03	Insult you, or humiliate you, or try to make you feel guilty				

Did an adult or older person ever involve you in any unwanted incidents of the following types before you reached the age of 16?

		Never	Once	Several Times	Often
04a	Touching or fondling your private parts				
04b	Made you touch them in a sexual way				
04c	Attempted or completed intercourse				
04d	Any other unwanted contact				
04e	Any other unwanted sexual activities that did not involve contact?				

Parental Bonding Instrument

The questions below list various attitudes and behaviours of your MOTHER. As you may remember your mother in your first 16 years would you place a tick in the most appropriate box next to each question:

		Very like	Moderately like	Moderately unlike	Very unlike
R3	She spoke to be in a warm friendly voice				
R4	She seemed emotionally cold to me				
R5	She appeared to understand my problems and worries				
R6	She enjoyed talking things over with me				
R7	She frequently smiled at me				
R8	She could make me feel better when I was upset				
R9	She talked with me very little				

Appendix 3 – North Staffordshire Osteoarthritis Project questionnaire

Demographic Information

Part 9 About You: Here are some general questions about yourself. Please follow the instructions and answer ALL of the following questions.

1 What is your date of birth? ☐☐ ☐☐ ☐☐☐☐

2 Are you Male ☐ Female ☐

3 What is your current marital status? (Please put a cross in one box only)

Married ☐ Widowed ☐
Separated ☐ cohabiting ☐
Divorced ☐ Single ☐

4 Do you live alone? Yes ☐ No ☐

5 What is your current employment status? (Please put a cross in one box only)

Employed ☐
Not working due of ill health ☐
Retired ☐
Unemployed / seeking work ☐
Housewife ☐
Other ☐

10 What is your current smoking status? (Please put a cross in one box only)

Never smoked ☐
Previously smoked ☐
Currently smoking ☐

11. On average, how often do you drink alcohol? (Please put a cross in one box only)

Daily or most days	Once or twice a week	Once or twice a month	Once or twice a year	Never
☐	☐	☐	☐	☐

12 How old were your when you left school? ☐☐ years

Social Network

Part 5 Friends and Family: We are interested in the contact you may have with your friends and family. Please answer each question and put a cross in one box for each line.

1. How often do you go to religious meetings or services?

More than once a week	Once a week	1 to 3 times per month	Less than once per month	Never or almost never
☐	☐	☐	☐	☐

2. How many hours **each week** do you participate in any groups such as social or work group, church-connected group, self-help group, charity, public service or community group?

None	1 to 2 hours	3 to 5 hours	6 to 10 hours	11 to 15 hours	16 or more hours
☐	☐	☐	☐	☐	☐

3. How many living children do you have?

None	1 to 2	3 to 5	6 or more
☐	☐	☐	☐

4. **How many of your children** do see at least **once a month**?

None	1 to 2	3 to 5	6 or more
☐	☐	☐	☐

5. Apart from your children, how many relatives do you have with whom you feel close?

None	1 to 2	3 to 5	6 to 10	10 or more
☐	☐	☐	☐	☐

6. **How many close relatives** do you see at least **once a month**?

None	1 to 2	3 to 5	6 to 10	10 or more
☐	☐	☐	☐	☐

7. How many close friends do you have?

None	1 to 2	3 to 5	6 to 10	10 or more
☐	☐	☐	☐	☐

8. **How many of these friends** do you see at least **once a month**?

None	1 to 2	3 to 5	6 to 10	10 or more
☐	☐	☐	☐	☐

9 Is there any one special person you know that you feel very close to; someone you feel you can share confidences and feelings with? Yes ☐ No ☐

If yes, how often do you see or talk with this person?

Daily	Weekly	Monthly	Several times a year	Once a year or less
☐	☐	☐	☐	☐

Hospital Anxiety and Depression Scale

The next set of questions are about how you feel at the moment. Please read each item and put a cross next to the reply that comes closest to how you have been feeling **in the past week**. Don't take too long over your replies; your immediate reaction to each item will usually be more accurate than a long thought out response.

1. I feel tense or 'wound up':

Most of the time	A lot of the time	From time to time, occasionally	Not at all
☐	☐	☐	☐

2. I still enjoy the things I used to enjoy:

Definitely as much	Not quite so much	Only a little	Hardly at all
☐	☐	☐	☐

3. I get a sort of frightened feeling as if something awful is about to happen:

Very definitely and quite badly	Yes, but not too badly	A little, but it doesn't worry me	Not at all
☐	☐	☐	☐

4. I can laugh and see the funny side of things:

As much as I always could	Not quite so much now	Definitely not so much now	Not at all
☐	☐	☐	☐

5. Worrying thoughts go through my mind:

A great deal of the time	A lot of the time	Not too often	Very little
☐	☐	☐	☐

6. I feel cheerful:

Never	Not often	Sometimes	Most of the time
☐	☐	☐	☐

7. I can sit at ease and feel relaxed:

Definitely	Usually	Not often	Not at all
☐	☐	☐	☐

8. I feel as if I am slowed down:

Nearly all the time	Very often	Sometimes	Not at all
☐	☐	☐	☐

9. I get a sort of frightened feeling like 'butterflies in the stomach:

Not at all	Occasionally	Quite often	Very often
☐	☐	☐	☐

10. I have lost interest in my appearance:

Definitely	I don't take as much care as I should	I may not take quite as much care	I take just as much care as ever
☐	☐	☐	☐

11. I feel restless as if I have to be on the move:

Very much indeed	Quite a lot	Not very much	Not at all
☐	☐	☐	☐

12. I look forward with enjoyment to things:

As much as I ever did	Rather less that I used to	Definitely less than I used to	Hardly at all
☐	☐	☐	☐

13. I get sudden feelings of panic:

Very often indeed	Quite often	Not very often	Not at all
☐	☐	☐	☐

14. I can enjoy a good book or radio or television programme:

Often	Sometimes	Not often	Very seldom
☐	☐	☐	☐

Illness perceptions questionnaire – revised; personal control scale

Please put a cross in one box on each line:

		Strongly agree	Disagree	Neither agree or disagree	Agree	Strongly agree
a	There is a lot which I can do to control my health	☐	☐	☐	☐	☐
b	I do will affect whether my health gets better or worse	☐	☐	☐	☐	☐
f	The course of my life depends on me	☐	☐	☐	☐	☐
g	I have the power to influence what happens in my life	☐	☐	☐	☐	☐

Sleep

Thinking over the **past 4 weeks**, did you?

		Not at all	On some nights	On most nights
4a	Have trouble falling asleep	☐	☐	☐
4b	Wake up several times per night	☐	☐	☐
4c	Have trouble staying asleep	☐	☐	☐
4d	Wake up after your usual amount of sleep feeling tired and worn out	☐	☐	☐

Pain

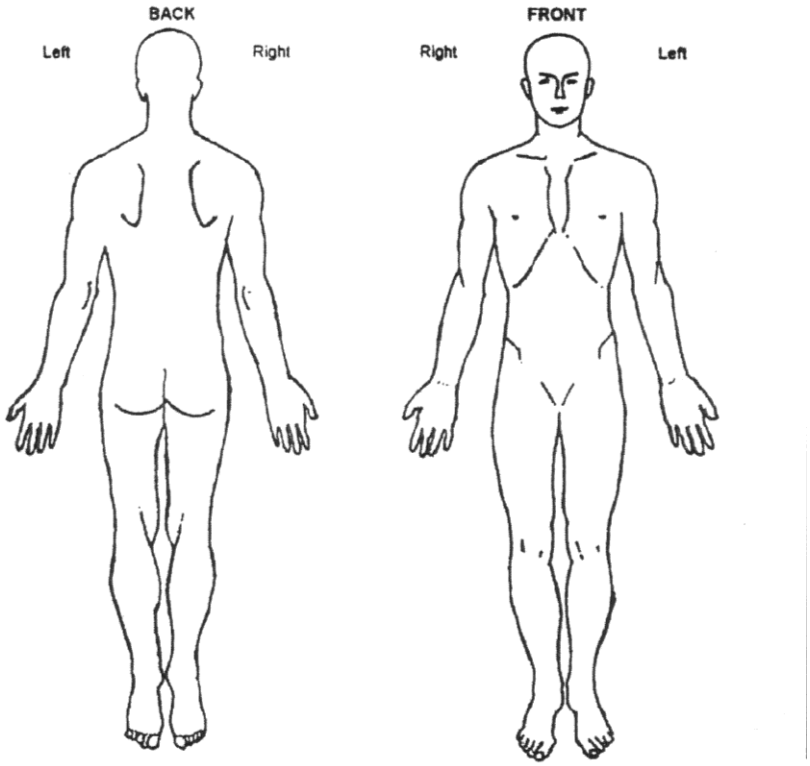
Part 1 - Body Chart

This question is about any **recent pain** you may have had in **any part of your body**. By pain we also mean ache, discomfort or stiffness. Please **do not** include pain due to a feverish illness such as flu. If you are a woman please **do not** include pain related to your monthly period.

1. In the **past 4 weeks**, have you had pain that has lasted for **one day or longer** in **any part of your body**?

Yes ..... ☐ Please shade in the diagram below **any pain** that has lasted for **one day or longer in the past 4 weeks**

No ..... ☐ Please turn the page over and continue with **Part 2.**



Appendix 4 – GPSS Results tables

Page

Table A4.1 Psychological stress and number of pain sites at baseline mediated by dismissing attachment style and moderated by childhood abuse and sex

			B	95% CI		P	B	R^2	a	b	Model Fit	
All	No abuse	Indirect	0.001	-0.001	0.009	0.271	0.001	0.213	0.046	0.021		
		Direct	0.450	0.324	0.564	0.001	0.656		(-0.033, 0.122)	(-0.041, 0.093)	RMSEA	0.036
		Total	0.451	0.327	0.566	0.001	0.657				SRMR	0.0506
	Abuse	Indirect	0.001	-0.003	0.012	0.468	0.001	0.201	0.032	0.019		
		Direct	0.449	0.300	0.593	0.001	0.806		(-0.086, 0.156)	(-0.075, 0.112)		
		Total	0.449	0.301	0.594	0.001	0.807					
	Frequent Abuse	Indirect	0.001	-0.001	0.008	0.325	0.001	0.335	0.065	0.012		
		Direct	0.573	0.432	0.708	0.001	0.872		(-0.064, 0.194)	(-0.024, 0.048)		
		Total	0.574	0.433	0.708	0.001	0.874					
Males	No abuse	Indirect	0.000	-0.008	0.005	0.842	0.000	0.295	-0.006	0.027		
		Direct	0.531	0.355	0.692	<0.001	0.728		(-0.118, 0.099)	(-0.064, 0.124)		
		Total	0.530	0.356	0.689	<0.001	0.728					
	Abuse	Indirect	0.001	-0.010	0.022	0.598	0.001	0.101	0.060	0.011		
		Direct	0.319	0.088	0.578	0.013	0.575		(-0.104, 0.228)	(-0.118, 0.138)		
		Total	0.319	0.090	0.578	0.012	0.576					
	Frequent Abuse	Indirect	0.000	-0.019	0.018	0.916	0.000	0.417	0.042	-0.002		
		Direct	0.664	0.424	0.825	0.001	1.096		(-0.159, 0.247)	(-0.147, 0.155)		
		Total	0.664	0.429	0.824	0.001	1.096					
Females	No abuse	Indirect	0.002	-0.007	0.018	0.458	0.003	0.142	0.104	0.020		
		Direct	0.365	0.198	0.543	0.001	0.559		(0.000, 0.214)	(-0.075, 0.113)		
		Total	0.367	0.201	0.546	0.001	0.562					
	Abuse	Indirect	0.000	-0.012	0.016	0.802	0.000	0.313	0.004	0.034		
		Direct	0.562	0.372	0.694	0.001	1.015		(-0.174, 0.185)	(-0.092, 0.159)		
		Total	0.562	0.378	0.696	0.001	1.015					
	Frequent Abuse	Indirect	0.000	-0.015	0.020	0.791	0.000	0.281	0.097	0.003		
		Direct	0.503	0.315	0.677	0.001	0.727		(-0.086, 0.264)	(-0.116, 0.124)		
		Total	0.503	0.315	0.674	0.001	0.727					

Analysis based on 1,443 participants: No abuse = 702, Abuse = 406, Frequent Abuse = 335. Males = 611: No abuse = 288, Abuse = 179, Frequent Abuse = 144. Females = 832: No abuse = 414, Abuse = 227, Frequent Abuse = 191. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.2 Psychological stress and number of pain sites at baseline mediated by social support and moderated by childhood abuse and sex

			β	β 95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.006	-0.029	0.008	0.369	-0.008	0.213	-0.157	0.035		
		Direct	0.455	0.333	0.572	0.001	0.666		(-0.280, -0.049)	(-0.074, 0.117)	RMSEA	0.059
		Total	0.449	0.333	0.566	0.001	0.658				SRMR	0.0472
	Abuse	Indirect	-0.002	-0.031	0.016	0.677	-0.004	0.202	-0.195	0.012		
		Direct	0.453	0.290	0.591	0.001	0.823		(-0.331, -0.063)	(-0.086, 0.1112)		
		Total	0.451	0.297	0.588	0.001	0.819					
	Frequent Abuse	Indirect	0.005	-0.027	0.042	0.699	0.007	0.333	-0.248	-0.018		
		Direct	0.567	0.416	0.701	0.001	0.867		(-0.388, -0.095)	(-0.139, 0.107)		
		Total	0.572	0.423	0.699	0.001	0.874					
Males	No abuse	Indirect	-0.018	-0.077	0.009	0.244	-0.024	0.303	-0.226	0.078		
		Direct	0.549	0.439	0.663	0.001	0.765		(-0.411, -0.034)	(-0.079, 0.204)		
		Total	0.532	0.420	0.645	0.001	0.740					
	Abuse	Indirect	-0.014	-0.079	0.007	0.237	-0.027	0.150	-0.208	0.067		
		Direct	0.396	0.287	0.498	0.002	0.765		(-0.414, 0.018)	(-0.065, 0.197)		
		Total	0.382	0.274	0.493	0.001	0.738					
	Frequent abuse	Indirect	0.030	-0.015	0.136	0.208	0.045	0.296	-0.254	-0.120		
		Direct	0.517	0.405	0.649	0.001	0.765		(-0.469, -0.019)	(-0.330, 0.104)		
		Total	0.547	0.434	0.670	0.001	0.810					
Females	No abuse	Indirect	-0.001	-0.020	0.011	0.671	-0.001	0.207	-0.081	0.009		
		Direct	0.448	0.385	0.514	<0.001	0.765		(-0.221, 0.051)	(-0.126, 0.115)		
		Total	0.447	0.383	0.512	<0.001	0.763					
	Abuse	Indirect	-0.011	-0.006	0.059	0.224	-0.017	0.231	-0.179	-0.059		
		Direct	0.467	0.375	0.552	0.001	0.765		(-0.363, -0.028)	(-0.193, 0.061)		
		Total	0.478	0.391	0.561	0.001	0.782					
	Frequent abuse	Indirect	-0.007	-0.054	0.022	0.490	-0.011	0.292	-0.238	0.031		
		Direct	0.520	0.440	0.611	<0.001	0.765		(-0.421, -0.045)	(-0.102, 0.156)		
		Total	0.512	0.421	0.606	<0.001	0.754					

Analysis based on 1,443 participants: No abuse = 702, Abuse = 406, Frequent Abuse = 335. Males = 611: No abuse = 288, Abuse = 179, Frequent Abuse = 144. Females = 832: No abuse = 414, Abuse = 227, Frequent Abuse = 191. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.3 Psychological stress and number of pain sites at baseline mediated by health anxiety and moderated by childhood abuse and sex

			β	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	0.000	-0.003	0.009	0.532	0.000	0.207	0.015	0.018		
		Direct	0.445	0.300	0.574	0.001	0.659		(-0.080, 0.115)	(-0.061, 0.102)	RMSEA	0.038
		Total	0.445	0.301	0.576	0.001	0.659				SRMR	0.0516
	Abuse	Indirect	-0.002	-0.027	0.003	0.362	-0.004	0.164	0.056	-0.038		
		Direct	0.405	0.198	0.588	0.001	0.723		(-0.059, 0.190)	(-0.149, 0.084)		
		Total	0.403	0.194	0.588	0.001	0.720					
	Frequent Abuse	Indirect	-0.002	-0.023	0.008	0.519	-0.002	0.300	-0.020	0.082		
		Direct	0.548	0.373	0.707	0.001	0.812		(-0.154, 0.119)	(-0.036, 0.219)		
		Total	0.546	0.373	0.705	0.001	0.810					
Males	No abuse	Indirect	0.002	-0.005	0.020	0.393	0.003	0.340	-0.067	-0.027		
		Direct	0.577	0.401	0.709	0.001	0.806		(-0.201, 0.064)	(-0.131, 0.088)		
		Total	0.579	0.405	0.708	0.001	0.809					
	Abuse	Indirect	-0.006	-0.090	0.029	0.611	-0.012	0.059	0.242	-0.025		
		Direct	0.253	-0.056	0.598	0.120	0.484		(0.007, 0.474)	(-0.204, 0.198)		
		Total	0.247	-0.055	0.606	0.119	0.472					
	Frequent Abuse	Indirect	0.002	-0.012	0.045	0.403	0.002	0.334	0.039	0.043		
		Direct	0.604	0.337	0.819	0.001	0.894		(-0.196, 0.272)	(-0.164, 0.224)		
		Total	0.606	0.346	0.822	0.001	0.896					
Females	No abuse	Indirect	0.006	-0.003	0.038	0.220	0.009	0.105	0.094	0.065		
		Direct	0.292	0.064	0.558	0.019	0.439		(-0.043, 0.242)	(-0.051, 0.201)		
		Total	0.298	0.068	0.560	0.017	0.449					
	Abuse	Indirect	0.000	-0.014	0.016	0.754	0.000	0.244	-0.004	-0.043		
		Direct	0.484	0.227	0.676	0.003	0.815		(-0.154, 0.163)	(-0.192, 0.120)		
		Total	0.485	0.232	0.676	0.002	0.815					
	Frequent Abuse	Indirect	-0.009	-0.050	0.008	0.212	-0.014	0.281	-0.079	0.119		
		Direct	0.510	0.259	0.716	0.001	0.768		(-0.242, 0.106)	(-0.063, 0.303)		
		Total	0.501	0.247	0.704	0.001	0.754					

Analysis based on 906 participants: No abuse = 456, Abuse = 211, Frequent Abuse = 239. Males = 379: No abuse = 187, Abuse = 89, Frequent Abuse = 103. Females = 527: No abuse = 269, Abuse = 122, Frequent Abuse = 136. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.4 Psychological stress and number of pain sites at baseline mediated by somatosensory amplification and moderated by childhood abuse and sex

			B	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	0.000	-0.010	0.008	0.942	0.000	0.206	-0.077	0.001		
		Direct	0.445	3.010	0.577	0.001	0.660		(-0.184, 0.033)	(-0.084, 0.089)	RMSEA	0.037
		Total	0.445	0.302	0.577	0.001	0.659				SRMR	0.0502
	Abuse	Indirect	-0.001	-0.019	0.007	0.659	-0.001	0.164	-0.044	0.014		
		Direct	0.404	0.194	0.587	0.001	0.723		(-0.187, 0.121)	(-0.099, 0.136)		
		Total	0.403	0.195	0.586	0.001	0.722					
	Frequent Abuse	Indirect	0.000	-0.006	0.014	0.584	0.000	0.294	-0.014	-0.023		
		Direct	0.547	0.374	0.706	0.001	0.811		(-0.172, 0.145)	(-0.132, 0.082)		
		Total	0.547	0.375	0.707	0.001	0.811					
Males	No abuse	Indirect	-0.004	-0.038	0.021	0.757	-0.006	0.341	-0.210	0.020		
		Direct	0.584	0.405	0.722	0.001	0.818		(-0.344, -0.070)	(-0.113, 0.142)		
		Total	0.580	0.405	0.709	0.001	0.812					
	Abuse	Indirect	0.004	-0.016	0.064	0.449	0.007	0.066	0.109	0.036		
		Direct	0.255	-0.071	0.618	0.134	0.484		(-0.106, 0.338)	(-0.167, 0.222)		
		Total	0.259	-0.047	0.611	0.104	0.491					
	Frequent Abuse	Indirect	-0.002	-0.046	0.023	0.801	-0.003	0.333	0.107	-0.016		
		Direct	0.609	0.341	0.824	0.001	0.901		(-0.154, 0.334)	(-0.194, 0.151)		
		Total	0.607	0.352	0.827	0.001	0.898					
Females	No abuse	Indirect	0.000	-0.010	0.020	0.762	0.000	0.100	0.047	0.007		
		Direct	0.298	0.070	0.560	0.016	0.449		(-0.107, 0.212)	(-0.114, 0.135)		
		Total	0.298	0.071	0.557	0.016	0.449					
	Abuse	Indirect	0.000	-0.032	0.024	0.934	-0.001	0.242	-0.137	0.003		
		Direct	0.483	0.222	0.678	0.003	0.813		(-0.314, 0.081)	(-0.145, 0.156)		
		Total	0.483	0.228	0.674	0.003	0.812					
	Frequent Abuse	Indirect	0.004	-0.015	0.049	0.458	0.006	0.267	-0.124	-0.032		
		Direct	0.499	0.244	0.709	0.001	0.750		(-0.326, 0.073)	(-0.212, 0.129)		
		Total	0.503	0.246	0.706	0.001	0.756					

Analysis based on 906 participants: No abuse = 456, Abuse = 211, Frequent Abuse = 239. Males = 379: No abuse = 187, Abuse = 89, Frequent Abuse = 103. Females = 527: No abuse = 269, Abuse = 122, Frequent Abuse = 136. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.5 Psychological stress and number of pain sites at baseline mediated by dissociation and moderated by childhood abuse and sex

			B	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	0.000	-0.003	0.007	0.559	0.000	0.206	-0.007	-0.018		
		Direct	0.445	0.299	0.577	0.001	0.659		(-0.095, 0.079)	(-0.018, -0.100)	RMSEA	0.039
		Total	0.445	0.300	0.577	0.001	0.660				SRMR	0.0511
	Abuse	Indirect	-0.002	-0.028	0.014	0.592	-0.004	0.162	0.140	-0.014		
		Direct	0.403	0.199	0.585	0.001	0.720		(-0.023, 0.310)	(-0.134, 0.107)		
		Total	0.401	0.194	0.583	0.001	0.716					
	Frequent Abuse	Indirect	0.000	-0.002	0.007	0.481	0.000	0.294	-0.016	-0.015		
		Direct	0.547	0.373	0.706	0.001	0.811		(-0.103, 0.073)	(-0.089, 0.095)		
		Total	0.547	0.374	0.706	0.001	0.812					
Males	No abuse	Indirect	0.000	-0.013	0.009	0.965	0.000	0.340	-0.021	0.012		
		Direct	0.551	0.403	0.709	0.001	0.738		(-0.153, 0.103)	(-0.125, 0.177)		
		Total	0.551	0.406	0.708	0.001	0.737					
	Abuse	Indirect	-0.019	-0.102	0.008	0.203	-0.035	0.073	0.169	-0.112		
		Direct	0.268	-0.049	0.605	0.096	0.503		(-0.098, 0.399)	(-0.278, 0.116)		
		Total	0.249	-0.082	0.601	0.145	0.467					
	Frequent Abuse	Indirect	0.000	-0.013	0.023	0.835	0.000	0.333	0.022	0.003		
		Direct	0.607	0.345	0.829	0.001	0.899		(-0.150, 0.224)	(-0.130, 0.156)		
		Total	0.607	0.351	0.828	0.001	0.899					
Females	No abuse	Indirect	0.000	-0.011	0.008	0.986	0.000	0.099	0.002	-0.034		
		Direct	0.297	0.067	0.562	0.020	0.447		(-0.117, 0.139)	(-0.128, 0.085)		
		Total	0.297	0.064	0.559	0.021	0.447					
	Abuse	Indirect	0.008	-0.008	0.062	0.279	0.013	0.248	0.124	0.061		
		Direct	0.477	0.219	0.678	0.001	0.805		(-0.114, 0.368)	(-0.082, 0.220)		
		Total	0.485	0.235	0.678	0.001	0.818					
	Frequent Abuse	Indirect	0.001	-0.009	0.009	0.622	0.001	0.266	-0.053	-0.010		
		Direct	0.501	0.236	0.702	0.001	0.756		(-0.155, 0.063)	(-0.099, 0.140)		
		Total	0.501	0.242	0.705	0.001	0.757					

Analysis based on 906 participants: No abuse = 456, Abuse = 211, Frequent Abuse = 239. Males = 379: No abuse = 187, Abuse = 89, Frequent Abuse = 103. Females = 527: No abuse = 269, Abuse = 122, Frequent Abuse = 136. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.6 Psychological stress and number of pain sites at follow up mediated by secure attachment style and moderated by childhood abuse and sex

			β	β 95% CI		P	B	R^2	a	B	Model fit	
All	No abuse	Indirect	-0.005	-0.027	0.012	0.543	-0.007	0.367	-0.203	0.024		
		Direct	0.288	0.156	0.430	<0.001	0.444		(-0.318, -0.088)	(-0.065, 0.105)	RMSEA	0.027
		Total	0.283	0.149	0.423	<0.001	0.436				SRMR	0.0535
	Abuse	Indirect	-0.014	-0.055	0.002	0.111	-0.022	0.333	-0.172	0.08		
		Direct	0.318	0.122	0.533	0.001	0.517		(-0.319, -0.017)	(-0.032, 0.186)		
		Total	0.305	0.114	0.529	0.002	0.495					
	Frequent Abuse	Indirect	-0.004	-0.063	0.047	0.806	-0.006	0.400	-0.442	0.010		
		Direct	0.110	-0.041	0.276	0.154	0.161		(-0.586, -0.243)	(-0.100, 0.129)		
		Total	0.106	-0.036	0.260	0.145	0.155					
Males	No abuse	Indirect	-0.019	-0.068	0.006	0.151	-0.027	0.264	-0.241	0.079		
		Direct	0.379	0.150	0.602	0.004	0.539		(-0.404, -0.066)	(-0.042, 0.200)		
		Total	0.360	0.130	0.585	0.004	0.512					
	Abuse	Indirect	-0.019	-0.124	0.009	0.181	-0.030	0.348	-0.211	0.09		
		Direct	0.370	0.082	0.692	0.010	0.585		(-0.467, 0.018)	(-0.087, 0.294)		
		Total	0.350	0.081	0.667	0.010	0.555					
	Frequent Abuse	Indirect	-0.002	-0.079	0.066	0.809	-0.003	0.424	-0.343	0.006		
		Direct	0.174	-0.104	0.488	0.187	0.248		(-0.576, -0.078)	(-0.168, 0.183)		
		Total	0.172	-0.077	0.475	0.169	0.245					
Females	No abuse	Indirect	0.002	-0.021	0.027	0.768	0.003	0.469	-0.172	-0.011		
		Direct	0.231	0.086	0.388	0.002	0.378		(-0.322, -0.015)	(-0.121, 0.117)		
		Total	0.232	0.096	0.389	0.001	0.381					
	Abuse	Indirect	-0.015	-0.073	0.004	0.160	-0.025	0.323	-0.160	0.092		
		Direct	0.213	-0.060	0.483	0.128	0.359		(-0.345, 0.043)	(-0.044, 0.224)		
		Total	0.198	-0.074	0.464	0.143	0.334					
	Frequent Abuse	Indirect	-0.006	-0.108	0.083	0.824	-0.010	0.389	-0.494	0.013		
		Direct	0.067	-0.146	0.340	0.533	0.107		(-0.684, -0.240)	(-0.161, 0.197)		
		Total	0.060	-0.134	0.282	0.548	0.097					

Analysis based on 737 participants: No abuse = 342, Abuse = 225, Frequent Abuse = 170. Males = 330: No abuse = 151, Abuse = 102, Frequent Abuse = 77. Females = 407: No abuse = 191, Abuse = 123, Frequent Abuse = 93. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.7 Psychological stress and number of pain sites at follow up mediated by social support and moderated by childhood abuse and sex

			β	β 95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	0.011	-0.023	0.073	0.521	0.018	0.369	-0.325	-0.035		
		Direct	0.269	0.138	0.409	0.001	0.419		(-0.504, -0.123)	(-0.167, 0.088)	RMSEA	0.028
		Total	0.281	0.143	0.415	0.001	0.437				SRMR	0.0548
	Abuse	Indirect	0.001	-0.016	0.036	0.654	0.002	0.332	-0.133	-0.009		
		Direct	0.307	0.093	0.529	0.006	0.513		(-0.342, 0.041)	(-0.156, 0.114)		
		Total	0.308	0.098	0.529	0.005	0.515					
	Frequent Abuse	Indirect	-0.016	-0.070	0.030	0.397	-0.024	0.401	-0.357	0.044		
		Direct	0.124	-0.034	0.289	0.124	0.186		(-0.526, -0.176)	(-0.090, 0.159)		
		Total	0.108	-0.038	0.256	0.142	0.162					
Males	No abuse	Indirect	0.064	-0.017	0.236	0.142	0.093	0.276	-0.485	-0.133		
		Direct	0.281	0.058	0.502	0.017	0.405		(-0.680, -0.152)	(-0.356, 0.051)		
		Total	0.346	0.091	0.547	0.014	0.498					
	Abuse	Indirect	0.007	-0.018	0.092	0.503	0.012	0.377	-0.048	-0.146		
		Direct	0.335	0.068	0.651	0.011	0.548		(-0.344, 0.175)	(-0.363, 0.014)		
		Total	0.342	0.071	0.646	0.013	0.560					
	Frequent abuse	Indirect	-0.022	-0.166	0.028	0.285	-0.032	0.424	-0.366	0.061		
		Direct	0.198	-0.099	0.546	0.201	0.287		(-0.672, -0.113)	(-0.123, 0.250)		
		Total	0.175	-0.083	0.494	0.180	0.255					
Females	No abuse	Indirect	-0.005	-0.048	0.010	0.395	-0.008	0.472	-0.131	0.039		
		Direct	0.238	0.092	0.387	0.001	0.392		(-0.338, 0.054)	(-0.107, 0.186)		
		Total	0.233	0.091	0.383	0.001	0.383					
	Abuse	Indirect	-0.021	-0.131	0.003	0.124	-0.036	0.323	-0.194	0.106		
		Direct	0.246	-0.062	0.519	0.118	0.424		(-0.542, 0.042)	(-0.060, 0.275)		
		Total	0.225	-0.067	0.487	0.126	0.388					
	Frequent abuse	Indirect	-0.013	-0.090	0.058	0.528	-0.022	0.39	-0.343	0.038		
		Direct	0.074	-0.139	0.309	0.481	0.124		(-0.578, -0.094)	(-0.173, 0.199)		
		Total	0.061	-0.134	0.276	0.538	0.102					

Analysis based on 737 participants: No abuse = 342, Abuse = 225, Frequent Abuse = 170. Males = 330: No abuse = 151, Abuse = 102, Frequent Abuse = 77. Females = 407: No abuse = 191, Abuse = 123, Frequent Abuse = 93. β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; R^2 = multiple squared correlation; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value $p<0.006$.

Table A4.8 Psychological stress and number of pain sites at follow up mediated by health anxiety and moderated by childhood abuse and sex

			β	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.006	-0.032	0.010	0.376	-0.011	0.200	-0.046	0.132		
		Direct	0.423	0.233	0.585	0.001	0.734		(-0.169, 0.099)	(0.018, 0.258)	RMSEA	0.029
		Total	0.417	0.221	0.582	0.001	0.723				SRMR	0.0503
	Abuse	Indirect	0.000	-0.029	0.016	0.861	-0.001	0.312	0.047	-0.008		
		Direct	0.559	0.232	0.737	0.001	1.106		(-0.118, 0.252)	(-0.192, 0.148)		
		Total	0.559	0.232	0.739	0.002	1.105					
	Frequent Abuse	Indirect	0.001	-0.015	0.049	0.602	0.002	0.071	0.016	0.091		
		Direct	0.225	-0.003	0.428	0.052	0.337		(-0.144, 0.196)	(-0.094, 0.334)		
		Total	0.226	-0.012	0.428	0.060	0.339					
Males	No abuse	Indirect	-0.012	-0.056	0.006	0.141	-0.019	0.130	-0.128	0.095		
		Direct	0.357	0.081	0.611	0.009	0.569		(-0.294, .067)	(-0.089, 0.246)		
		Total	0.345	0.074	0.606	0.010	0.550					
	Abuse	Indirect	0.000	-0.051	0.033	0.948	-0.001	0.419	0.026	-0.013		
		Direct	0.644	0.297	0.887	0.001	0.159		(-0.231, 0.331)	(-0.285, 0.175)		
		Total	0.643	0.289	0.883	0.001	1.587					
	Frequent Abuse	Indirect	-0.003	-0.091	0.029	0.623	-0.004	0.111	0.059	-0.055		
		Direct	0.315	-0.121	0.621	0.137	0.358		(-0.315, 0.374)	(-0.282, 0.204)		
		Total	0.312	-0.113	0.611	0.134	0.355					
Females	No abuse	Indirect	0.006	-0.015	0.082	0.408	0.011	0.264	0.045	0.130		
		Direct	0.474	0.198	0.675	0.003	0.879		(-0.142, 0.274)	(-0.043, 0.311)		
		Total	0.480	0.204	0.675	0.004	0.890					
	Abuse	Indirect	0.000	-0.041	0.085	0.764	0.001	0.150	0.071	0.006		
		Direct	0.356	-0.073	0.749	0.114	0.516		(-0.168, 0.407)	(-0.276, 0.332)		
		Total	0.357	-0.067	0.745	0.102	0.517					
	Frequent Abuse	Indirect	-0.011	-0.105	0.019	0.305	-0.021	0.064	-0.067	0.162		
		Direct	0.193	-0.138	0.487	0.229	0.374		(-0.269, 0.180)	(-0.108, 0.444)		
		Total	0.182	-0.153	0.471	0.272	0.353					

Analysis based on 468 participants: No abuse = 226, Abuse = 116, Frequent Abuse 126. Males = 201: No abuse = 96, Abuse = 47, Frequent Abuse = 58. Females = 267, No abuse = 130, Abuse = 69), Frequent Abuse = 68). β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.9 Psychological stress and number of pain sites at follow up mediated by somatosensory amplification and moderated by childhood abuse and sex

			B	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	-0.009	-0.040	0.009	0.252	-0.015	0.200	-0.069	0.125		
		Direct	0.427	0.240	0.595	0.001	0.737		(-0.210, 0.089)	(0.006, 0.260)	RMSEA	0.029
		Total	0.419	0.23	0.584	0.001	0.723				SRMR	0.0480
	Abuse	Indirect	-0.005	-0.068	0.011	0.445	-0.011	0.319	0.14	-0.038		
		Direct	0.569	0.250	0.746	0.001	1.157		(-0.051, 0.357)	(-0.231, 0.127)		
		Total	0.564	0.251	0.740	0.002	1.146					
	Frequent Abuse	Indirect	0.001	-0.015	0.031	0.643	0.001	0.061	0.094	0.009		
		Direct	0.221	-0.019	0.424	0.073	0.332		(-0.106, 0.289)	(-0.142, 0.154)		
		Total	0.222	-0.013	0.423	0.063	0.334					
Males	No abuse	Indirect	-0.017	-0.082	0.007	0.173	-0.026	0.140	-0.140	0.119		
		Direct	0.367	0.101	0.635	0.005	0.582		(-0.315, 0.034)	(-0.095, 0.330)		
		Total	0.351	0.087	0.611	0.009	0.556					
	Abuse	Indirect	0.004	-0.031	0.076	0.469	0.009	0.418	0.133	0.026		
		Direct	0.638	0.260	0.872	0.001	1.584		(-0.141, 0.457)	(-0.261, 0.270)		
		Total	0.642	0.298	0.886	<0.001	1.593					
	Frequent Abuse	Indirect	-0.017	-0.168	0.034	0.460	-0.019	0.113	0.249	-0.068		
		Direct	0.323	-0.132	0.613	0.142	0.367		(-0.118, 0.532)	(-0.325, 0.215)		
		Total	0.306	-0.099	0.606	0.124	0.348					
Females	No abuse	Indirect	0.000	-0.034	0.049	0.904	0.001	0.259	0.004	0.112		
		Direct	0.479	0.200	0.678	0.003	0.883		(-0.234, 0.266)	(-0.042, 0.279)		
		Total	0.480	0.199	0.672	0.004	0.884					
	Abuse	Indirect	-0.006	-0.109	0.018	0.504	-0.009	0.155	0.104	-0.06		
		Direct	0.366	-0.093	0.716	0.141	0.544		(-0.165, 0.438)	(-0.293, 0.205)		
		Total	0.360	-0.080	0.702	0.122	0.535					
	Frequent Abuse	Indirect	-0.003	-0.068	0.016	0.507	-0.006	0.045	-0.058	0.052		
		Direct	0.181	-0.170	0.467	0.296	0.347		(-0.320, 0.185)	(-0.142, 0.229)		
		Total	0.178	-0.156	0.459	0.279	0.342					

Analysis based on 468 participants: No abuse = 226, Abuse = 116, Frequent Abuse 126. Males = 201: No abuse = 96, Abuse = 47, Frequent Abuse = 58. Females = 267, No abuse = 130, Abuse = 69), Frequent Abuse = 68). β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Table A4.10 Psychological stress and number of pain sites at follow up mediated by dissociation and moderated by childhood abuse and sex

			B	95% CI		P	B	R^2	a	b	Model fit	
All	No abuse	Indirect	0.000	-0.011	0.012	0.829	0.000	0.182	-0.077	-0.003		
		Direct	0.418	0.228	0.586	0.001	0.724		(-0.180, 0.054)	(-0.114, 0.129)	RMSEA	0.032
		Total	0.418	0.225	0.585	0.001	0.724				SRMR	0.0503
	Abuse	Indirect	-0.001	-0.052	0.027	0.728	-0.002	0.310	0.091	-0.011		
		Direct	0.559	0.248	0.735	0.002	1.098		(-0.129, 0.293)	(-0.211, 0.208)		
		Total	0.558	0.236	0.734	0.002	1.096					
	Frequent Abuse	Indirect	-0.001	-0.013	0.007	0.753	-0.001	0.064	0.021	-0.025		
		Direct	0.227	-0.011	0.430	0.061	0.339		(-0.118, 0.151)	(-0.130, 0.120)		
		Total	0.227	-0.008	0.430	0.057	0.339					
Males	No abuse	Indirect	-0.003	-0.038	0.018	0.564	-0.005	0.120	-0.123	0.025		
		Direct	0.346	0.068	0.609	0.012	0.553		(-0.240, 0.031)	(-0.157, 0.241)		
		Total	0.343	0.075	0.603	0.009	0.548					
	Abuse	Indirect	-0.005	-0.167	0.050	0.600	-0.013	0.421	0.160	-0.033		
		Direct	0.650	0.330	0.893	0.001	1.587		(-0.124, 0.444)	(-0.403, 0.346)		
		Total	0.644	0.312	0.877	0.001	1.574					
	Frequent Abuse	Indirect	0.000	-0.340	0.043	0.990	0.000	0.111	0.018	0.022		
		Direct	0.310	-0.096	0.628	0.124	0.351		(-0.225, 0.323)	(-0.171, 0.295)		
		Total	0.311	-0.096	0.619	0.128	0.351					
Females	No abuse	Indirect	0.001	-0.010	0.023	0.446	0.002	0.246	-0.040	-0.025		
		Direct	0.482	0.201	0.677	0.002	0.893		(-0.215, 0.194)	(-0.179, 0.146)		
		Total	0.483	0.21	0.676	0.001	0.894					
	Abuse	Indirect	-0.001	-0.039	0.044	0.913	-0.001	0.151	0.02	-0.041		
		Direct	0.354	-0.093	0.701	0.129	0.518		(-0.353, 0.292)	(-0.221, 0.178)		
		Total	0.353	0.075	0.700	0.114	0.517					
	Frequent Abuse	Indirect	0.001	-0.009	0.024	0.442	0.002	0.042	-0.030	-0.038		
		Direct	0.173	-0.160	0.458	0.298	0.336		(-0.187, 0.219)	(-0.173, 0.151)		
		Total	0.174	-0.158	0.456	0.283	0.338					

Analysis based on 468 participants: No abuse = 226, Abuse = 116, Frequent Abuse 126. Males = 201: No abuse = 96, Abuse = 47, Frequent Abuse = 58. Females = 267, No abuse = 130, Abuse = 69), Frequent Abuse = 68). β = Standardized regression coefficient; 95% C.I. = Bias corrected confidence intervals based on bootstrap of 3000; B = Unstandardized regression coefficient; a = path from psychological stress to mediator; b = path from mediator to number of pain sites, critical value p<0.006.

Appendix 5 – Surgery read codes excluded

Category	Read Code	Read Code Term
Dermalogical	7G2E	Dressing of skin or wound
Feet	7	Operations, procedures, sites
Endocrine	7135	Biopsy of breast
Eye Op	7203	Attention to prosthesis of eye
Mouth Op	7512	Simple dental extraction
Nervous Sys	70560	Carpal tunnel release
Nervous Sys	70580	Cubital tunnel release
Nervous Sys	70652	Nerve conduction studies
Endocrine	71350	Needle guided breast biopsy
Eye Op	72110	Excision of lesion of canthus
Eye Op	72122	Cryotherapy to lesion of eyelid
Eye Op	72126	Incision and curettage of meibomian cyst
Eye Op	72131	Blepharoplasty of upper eyelid
Eye Op	72310	Recession med rectus eye NEC
Eye Op	72462	Removal of suture from cornea
Eye Op	72744	Fluorescein angiography of eye
Ear Op	73050	Irrig ext aud canal remov wax
Ear Op	73064	Irrigation ext aud canal NEC
Mouth Op	75121	Dental clearance NEC
Mouth Op	75140	Apicectomy of tooth
Digestive	77352	Injection of sclerosing substance into haemorrhoid
Genital F upper	7E005	Cervical polypectomy
Genital F upper	7E034	Colposcopy of cervix
Genital F upper	7E035	Colposcopic biopsy cervix
Genital F upper	7E094	Introduction of Mirena coil
Nervous Sys	704A	Therapeutic epidural injection
Nervous Sys	7063q	Chemical sympathectomy NEC
Digestive	773A1	Drainage of perianal abscess
Artery	7A551	Monitoring arterial pressure
Urinary	7B2B2	Removal of urethral catheter
Urinary	7B2Bz	Ureth catheterisation blad NOS
Urinary	7B2C1	Change of suprapubic catheter
Urinary	7B2C9	Insertion suprapubic catheter
Genital F lower	7D011	Marsupialisation of Bartholin gland
Genital F lower	7D1B	Intro support pess into vagina
Genital F lower	7D1C2	Colposcopy NEC
Genital F upper	7E0F1	Endometrial biopsy
Genital F upper	7E2A2	Cervical smear taken
Dermalogical	7G033	Excision lesion of skin NEC
Dermalogical	7G03312	Excision of papilloma
Dermalogical	7G035	Ligation of skin tag
Dermalogical	7G037	Excision of sebaceous cyst NEC
Dermalogical	7G03C	Excision mole skin head/neck
Dermalogical	7G05B	Excision biopsy of skin lesion
Dermalogical	7G05z	Excision of skin lesion NOS
Dermalogical	7G061	Curett cautery lesion skin NEC
Dermalogical	7G091	Cryotherapy skin lesion NEC
Dermalogical	7G0Cz	Other biopsy of skin NOS
Dermalogical	7G22	Removal of suture of skin
Dermalogical	7G255	Piercing of earlobe
Dermalogical	7G2A3	Inject therap subst subcut NEC
Dermalogical	7G2A5	Insertion of testosterone implant
Dermalogical	7G2A6	Insertion of hormone implant
Dermalogical	7G2E3	Dressing of skin NEC
Dermalogical	7G2E5	Dressing of skin ulcer NEC
Dermalogical	7G2E9	Attention dressing of skin NEC

Category	Read Code	Read Code Term
Dermalogical	7G2F1	Exploration of skin wound NEC
Dermalogical	7G321	Removal of nail NEC
Dermalogical	7G64	Excision Sebaceous Cyst
Dermalogical	7G65	Excision Lipoma
Dermalogical	7G67	Excision Papilloma
Soft Tissue	7H372	Excision of ganglion of knee
Soft Tissue	7H37z	Excision of ganglion NOS
Soft Tissue	7H62	Excision or biopsy of lymph node
Soft Tissue	7H626	Excis/biop inguinal lymph node
Soft Tissue	7H629	Supraclavicular lymph node biopsy
Bone	7J461	Injection around spinal facet NEC
Bone	7J5	Removal Of Foreign Bodies NOS
Bone	7K1L1	Manipulation of fracture of bone NEC
Bone	7K6a9	MUA - shoulder joint
Bone	7K6aC	MUA - hip joint
Bone	7K6F5	Pry opn red disloc alone
Bone	7K6Z0	Aspiration of joint
Bone	7K6Z2	Inject therap subst in joint
Bone	7K6Z3	Injection into joint NEC
Bone	7K6Z4	Injection into temporomandibular joint
Bone	7K6Z5	Injection of steroid into shoulder joint
Bone	7K6Z7	Injection of steroid into knee joint
Bone	7K6Z8	Aspiration of fluid from knee joint
Injection	7L11	Injection of therapeutic substance
Injection	7L121	Intravenous pyelography
Injection	7L17	Blood withdrawal
Injection	7L18	Intramuscular injection
Injection	7L19	Subcutaneous injection
Haemodialysis	7L1A2	Haemodialysis NEC
Immobilise	7L1F6	Application of functional brace
Immobilise	7L1G0	Application of splint NEC
Immobilise	7L1G7	Fitting of cervical collar
Heart	7L1H0	Direct current cardioversion
Heart	7L1H1	External cardioversion NEC
Organ Not Spec	7M0G5	Drainage of cyst NEC
Anaesthetic	7M340	Nerve block NEC
Anaesthetic	7M371	Radiotherapy NEC
Op Site	7N131	[SO]Skin of eyebrow
Op Site	7N133	[SO]Skin of eyelid
Op Site	7N710	[SO]Skin of scalp
Proc Complic	SP001	Mechanical complication of cardiac pacemaker
Proc Complic	SP047	Breakage of prosthesis
Proc Complic	SP079	Problem with vaginal pessary
Post Op	SP122	Post operative DVT
Post Op	SP212	Post-operative haematoma formation
Post Op	SP23z	Delayed healing surgical wound
Post Op	SP250	Postop. stitch abscess
Post Op	SP255	Postop. wound infectionunspec
Post Op	SP257	Post-op wound infectn-superfic
Post Op	SP2y2	Postoperative pain
Post Op	SP320	Phlebitis after infusion
Injury Poisoning	U6000	[X] Adv react to penicillins
Injury Poisoning	U6051	[X] Adverse react to aspirin
Injury Poisoning	U6053	[X]Ad reac non-ster ant-inflam
Injury Poisoning	U60G0	[X]Ad reac loc antinf/infl NOS

Appendix 6 – PhD related presentations

Woodward, A.D.; Campbell, P.; Creed, F.H.; Tomenson, B. & McBeth, J. (2013) *Childhood trauma, adult psychological status and pain: a conditional process analysis.* Poster presentation. European Federation of IASP Chapters Pain Congress, Florence.

Woodward, A.D.; Campbell, P.; Creed, F.H.; Tomenson, B. & McBeth, J. (2013) *Psychological stress and widespread pain: the moderating effect of childhood abuse.* Oral and poster presentations. British Pain Society Annual Scientific Meeting, Bournemouth. I was invited to speak and won first prize for the best trainee oral presentation.

Woodward, A.D. (2012) *Starting to find answers – collecting and making sense of quantitative information.* Oral presentation. Social Sciences: Improving care, Improving Lives. ESRC funded event.

Woodward, A.D.; Campbell, P.; Creed, F.H.; Tomenson, B. & McBeth, J. (2012) *Anxiety and chronic widespread pain: the moderating effect of childhood abuse.* Poster presentation. International Association for the Study of Pain 14th International Pain Congress, Milan.

Woodward, A.D.; Campbell, P.; Creed, F.H.; Tomenson, B. & McBeth, J. (2012) *Anxiety and chronic widespread pain: the moderating effect of childhood abuse.* Oral presentation. Primary Care Sciences Graduate Symposium – section prize winner.

Woodward, A. (2011) *Does Childhood Trauma Moderate the Risk of Developing Chronic Widespread Pain in Adulthood?* Poster presentation Keele University Graduate Symposium