

Chapter 1

GENERAL INTRODUCTION

This thesis aims to increase understanding of the predictors of adjustment to pain in an attempt to contribute to improved treatment outcomes and higher quality of life for patients with advanced cancer. Pain is one of the most feared and distressing symptoms of cancer for both patients and carers and it results in increased demand on scarce health services (Wagner-Johnstone, Carson, & Grossman, 2010). Past research has focused on pain characteristics as a predictor of adjustment. However, cancer patients receiving palliative care often report diverse levels of adjustment even when the characteristics of pain and the stage of their disease are similar. Despite this, comparatively little palliative care research focuses on factors (other than characteristics of the pain) that may influence adjustment to cancer pain. This thesis uses both qualitative and quantitative methods to examine relationships between cancer pain, other symptoms and psychological factors, and adjustment in samples derived from multiple sites. Archival and cross-sectional and longitudinal data from contemporary samples are used.

Defining Pain

It is necessary to define pain before attempting to examine its relationship to other variables. The International Association for the Study of Pain (IASP) (1986) described pain as:

“an unpleasant sensory experience and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (p. 217).

Pain has been classified in a number of ways (Table 1.1) (Bruera, MacMillan, Hanson, & MacDonald, 1989, Bruera et al., 1995; Caraceni & Portenoy 1999; Colleau, 2004; Fainsinger et al., 2005; Fine, Davies & Fishman, 2008; Mercadante, Arcuti, Tirelli, & Casuccio, 2000; Tywcross, 1997). For example, Caraceni and Portenoy (1999) distinguished between 22 types of cancer pain, in terms of its location and cause. Others have distinguished between short flare-ups of pain occurring on a background of otherwise controlled pain (breakthrough pain) and other types of pain, irrespective of its location or cause (e.g., Bhatnagar, Upadhyay & Mishra, 2009; Haugen, Hjermstad, Hagen, Caraceni, & Kaasa, 2010; Zeppetella, in press; Zeppetella, O’Doherty, & Collins, 2000).

Table 1.1
Most Commonly Used Classifications of Pain in Previous Research with Cancer Patients

Dimension on which pain is classified			
Temporal	Pathophysiology	Aetiology	Location
acute	nociceptive	due to cancer	site of pain
chronic	neuropathic	due to treatment	
incident	psychogenic	due to general illness	
breakthrough		non cancer pain	

These distinctions may be important for the development of effective treatments for cancer pain, however all categories of pain are likely to influence patient adjustment.

Because this thesis focuses on factors that influence pain and adjustment, it does not focus on the classification of patients' pain.

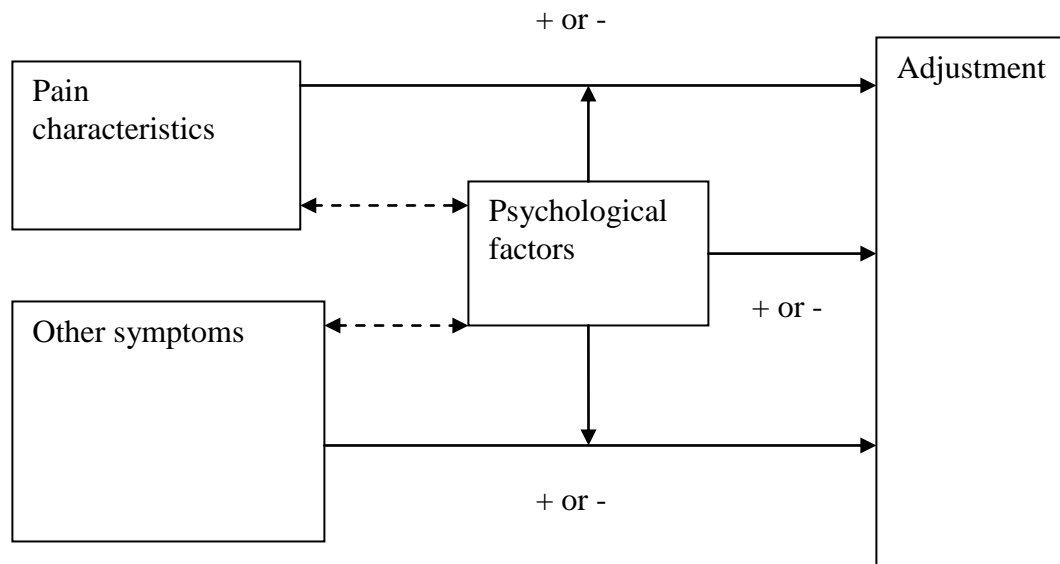
However, a large body of literature shows that characteristics of pain are associated with adjustment. This thesis focuses on three characteristics (frequency, duration and intensity) of pain experienced by patients with advanced cancer. The first study focuses on two of the characteristics, frequency and intensity, but incorporates all patient pain. In subsequent studies, "pain duration" is also examined, but the focus is narrowed to breakthrough pain because its unpredictable nature is expected to present a particular challenge to patient adjustment.

Pain Theories

There are a number of theories about pain perception. The most renowned theory of pain in psychological literature is the Gate Control Theory (Melzack & Wall, 1965). In its original form, this proposed that the perception of physical pain was the outcome of activity by two types of neurons: pain-transmitting and non-pain-transmitting.

Activation of non-pain-transmitting neurons can interfere with the signals between pain fibres and therefore inhibit pain perception (Melzack & Casey, 1968; Melzack & Wall, 1965). Melzack (1971) expanded the original theory to incorporate the Central Biasing Theory of pain modulation, in which cognitive, motivational and affective mechanisms in the cerebral cortex are involved in emotional responses to pain. Perceived pain, therefore, results from an interaction between sensory-physical, motivational-affective and cognitive-evaluative mechanisms. This theory underpins modern concepts of pain, which incorporate biological, psychological and social factors in a multidimensional

model of pain perception. One implication of these concepts is that perceived pain can be modified by a wide variety of factors, such as other symptoms, psychological factors, social difficulties, cultural issues and spiritual concerns (Gagliese, Gauthier & Rodin, 2007; Laird, Boyd, Calvin & Fallon, 2009; McGrath, 1999; Turk & Melzack, 2001; Utne, Miaskowski, Bjordal, Paul, & Rustoen, 2008, 2010; Valente, Ribeiro & Jenson, 2009; Watson & Homewood, 2008; Wing & Fielding, 2007; Woodruff, 1999), each of which can diminish or exacerbate perception of pain. However, these factors are not only likely to influence the perception of pain, but also adjustment to it. Following modern concepts of pain, this thesis explores the influence of pain characteristics, other potentially distressing symptoms and psychological factors on patient adjustment (Figure 1.1).



Legend_ \longrightarrow Relationships tested in this study
 \longleftrightarrow Possible relationships for which there were insufficient prior research to support a hypotheses.

Figure 1.1. Factors influencing adjustment to pain.

Adjustment

The concept of adjustment is first discussed before addressing the various factors which influence adjustment. Adjustment to illness refers to the psychological processes that occur over time as individuals and those in their social world, manage, learn from and adapt to the multitude of changes that have been precipitated by illness and its treatment (Brennan, 2001). The term adjustment has been used to define a number of aspects of the process of adaptation, however this thesis is concerned with only three of these: level of coping, quality of life and symptoms of depression.

Coping

The concept of coping was originally developed from appraisal theory (Arnold, 1960; Lazarus 1966) and was refined by Lazarus and Folkman (1984). Appraisal refers to the individual's evaluation of the personal significance of an event and the adequacy of the individual's resources to meet the demands of the event (Arnold, 1960; Lazarus 1966). Coping refers to the process of managing internal and external demands which are appraised as taxing or exceeding the resources of the individual (Lazarus & Folkman, 1984). That is, coping refers to efforts to manage and overcome demands and critical events that are perceived as a challenge, threat, harm, loss, or benefit to a person (Lazarus, 1992). It may involve thoughts and behaviours that a person uses to regulate distress (emotion-focused coping), the management of the problem causing distress (problem-focused coping) and the efforts to maintain well-being by reappraising the outcomes of earlier coping (meaning-based coping) (Folkman & Greer, 2000).

Several different ways of conceptualising the process of coping have emerged over time. Research concerning coping has focused on coping strategies (Brown & Nicassio, 1987; Greenglass, Schwarzer & Taubert, 1999; Lazarus & Folkman, 1984,1991; Reid, Gilbert, & McGrath, 1998; Riley et al., 1999; Rosenstiel & Keefe, 1983; Swartzman, Gwardry, Shapiro & Teasell, 1994; Schwarzer & Knoll, 2009), coping styles (Brandstander, 1992; Lazarus, 1991; Moos & Schaeffer, 1993; Watson, Greer, Young, Inayat, Burgess, & Robertson, 1988; Watson, Law, dos Santos, Greer, Baruch, & Bliss, 1994), and perceived self-efficacy for coping (Derogates & Lopez, 1983; Jalowiec, Murphy & Powers,1984; Lin, 1998; Lindquest & Sjoden, 1998; Merluzzi, Nairn, Hedge, Sanchez, & Dunn, 2001). In the context of illness, coping strategies are the various cognitive and behavioural techniques that individuals use to deal with the stress of illness and its consequences, and perceived self-efficacy for coping refers to the extent to which the patients believe their strategies use is effective. On the other hand, coping styles refer to the individual's enduring disposition to deal with challenges and stresses with a specific constellation of coping strategies. However, the style or strategy adopted by the patient, and third party judgements about the efficacy of these strategies or styles seem less important to patient adjustment than how well these ways of coping worked for the patient.

More recently, research on adjustment to pain has focused on one aspect of coping, namely acceptance. Acceptance in this context, is defined as coping with, coming to terms with, or dealing with pain (Chapelle, Lavoie & Boudreau, 2008) by giving up the struggle against pain and learning to live life despite pain (McCracken, Vowles &

Eccleston, 2004; Gauthier et al., 2009). These different ways of conceptualising coping have resulted in the development of a range of very different measures of coping.

Measuring Coping

Coping has been measured from the perspective of coping strategies, styles, self-efficacy for coping, and also one aspect of coping, acceptance. Many of the existing measures of coping are problematic for use with patients with advanced cancer for three reasons. First, most instruments are too lengthy to be tolerated in this population. For example, the most widely used measures of coping strategies involve 48 (*Coping Strategies Questionnaire* (Rosenstiel & Keefe 1983)) and 68 items (*Ways of Coping Scale* (Lazarus & Folkman, 1984)). The most widely used measures of coping styles are also long. The *Mental Adjustment to Cancer Scale* (MAC) (Watson et al., 1988) contains 40 items, and the shorter *mini-MAC* (Watson et al., 1994) still contains 29. Similarly, measures of effectiveness of coping strategies contain 46 (*Psychosocial Adjustment to Illness Scale* (Derogates & Lopez, 1983)), the *Self-efficacy for Coping with Cancer Scale* (Merluzzi, Nairn, Hedge, Sanchez & Dunn, 2001) contains 33 and the *Jalowiec Coping Scale* (Jalowiec et al., 1984) contains 40 items. Moreover, the *Jalowiec Coping Scale* (Jalowiec et al., 1984) assesses the perceived effectiveness of specific coping strategies and not overall level of coping. Although these measures have been used for assessing the use, styles and effectiveness of individual coping strategies in patients with cancer, many patients with advanced cancer would not be able to complete instruments of this length.

Second, these instruments were not designed to measure coping with terminal illness and contain many items which are not relevant the end of life. For example, the vocational domain of the *Psychosocial Adjustment to Illness Scale* (Derogates & Lopez, 1983) is unlikely to be relevant for many patients with advanced cancer. Moreover, implicit in these measures, is a judgement about which styles and strategies are adaptive. These judgements may not apply to stressors associated with a terminal illness, as well as to those associated with the other stressors for which the scales were designed (e.g., unemployment).

Third, only one measure related to coping has been validated in a population of patients with advanced cancer who are experiencing pain (Geiser, 1992). This measure, the *Chronic Pain Acceptance Questionnaire* (Geiser, 1992) was originally designed for use with patients with chronic pain but without malignant disease (e.g., patients with back injuries and rheumatoid arthritis) but it has recently been validated for use with patients with advanced cancer (Gauthier et al., 2009). Despite this, the instrument is too lengthy (20 items) to be tolerated by many patients with advanced cancer. These instruments are therefore unsuitable for measuring coping in most patients with advanced cancer.

Level of Coping. In this thesis, level of coping refers to the patient's overall perception of the extent to which he/she is coping as the sum outcome of the deployment of the variety of cognitive, behavioural, and emotional and social strategies in his/her repertoire. Most of the existing measures of coping actually assess coping

styles, strategies or the self-efficacy of the patients to use particular coping strategies rather than the patients' level of coping. This thesis focuses on "level of coping". Relatively few measures of effectiveness of coping efforts have been reported in the existing literature. However, a single-item measure has been used among students and older adults (Aldwin, 1991), patients with psychological conditions (Aldwin & Reversion, 1987), women with gastrointestinal disorders (Drossman, Lesserman, Zhiming, Keefe, Yuming, & Toomey, 2000) and the caregivers of patients with advanced disease (Fisher, 2008). Although it has not been validated among patients with advanced cancer, the single-item measure of perceived overall effectiveness of coping meets many of the other requirements of measures suitable for use among patients receiving palliative care.

Quality of Life

Quality of life is another domain of adjustment that is highly relevant for patients with advanced cancer. However, it has been proven to be a difficult concept to define and to measure (Calman, 1984; Rummans et al., 1998). Quality of life has been conceptualised in two ways that are relevant to this thesis: global quality of life and health-related quality of life. Global quality of life is defined as an overall evaluation of satisfaction with one's life (Calman, 1984; Cooley, 1998; Llobera et al., 2003; Nuamah, Cooley, Fawcett & Mc Corkle, 1999; Padilla et al., 1992; Rummans et al., 1998; Ventegodt, Merrick & Andersen, 2003) while health-related quality of life is an "all encompassing" concept, related to the impact of a medical condition or specific medical interventions on a person's physical, psychological and social well-being (Skeel, 1998). This thesis

assesses a global quality of life, because of its focus on a range of factors which are likely to influence adjustment. These factors may or may not be related to the medical condition or its treatment.

Measuring Quality of Life

Various instruments have been devised for the measurement of global quality of life. These include the *Quality of Life Index (QLI)* (Spitzer, Dobson, Hall, Chesterman et al., 1981), the *European Organization for Research and Treatment of Cancer QLQ-C30* (Aaronson, Ahmedzai, Bergman, Ballinger et al., 1993), the *McGill QOL Questionnaire* (Cohen, 1985), and the revised *McGill QOL Questionnaire* (Cohen, Mount, & Bruera, 1997). These assess multi-faceted concepts of quality of life which encompass physical, cognitive, emotional, social and existential domains of an individual's life. Although these measures have been validated among cancer patients, they are too lengthy for many patients with advanced disease. On the other hand, the *Hebrew Rehabilitation Center for Aged Quality of Life Index (HRCA-QL)* (Llobera et al., 2003) is a brief measure that has been validated and widely used in patients with advanced disease. It is a multidimensional measure that assesses global quality of life and was derived from the QLI (Spitzer et al., 1981). It contains five items that assess aspects of quality of life that are particularly important in the context of illness (mobility, daily living, health, support, outlook). Despite these advantages, the measure has some shortcomings. It does not encompass all relevant dimensions of quality of life. Specifically, social contact and emotional well-being are not assessed. Nevertheless, as the best available measure for this population, the HRCA-QL was adopted to assess this aspect of adjustment.

Symptoms of Depression

Mental health is also a dimension of adjustment with relevance to patients with advanced cancer. The presence of depression is identified by symptoms, such as depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration (World Health Organisation, 2011).

In particular, symptoms of depression are common among cancer patients with advanced disease (Edrington et al., 2010; Fischer, Villines, Kim, Epstein & Wilkie, 2010; Gagliese, Gauthier & Rodin, 2007; Laird, Boyd, Calvin & Fallon, 2009; McMillan, Tofthagen & Morgan, 2008).

Symptoms of depression are more prevalent among cancer patients with pain than among those without it (Finset & Wigers, 2004; Lin, Lai, & Ward, 2003; Spiegel, Sands & Koopman, 1994; Tavoli, Montazeri, Roshan, Tavoli & Melyani, 2008). In fact, in one study, 66% of cancer patients with pain reported symptoms of depression, which was sometimes accompanied by another co-morbid mental health problem (Utne, San, Miaskowski et al., 2010). This thesis therefore also explores the relationships between pain, psychological factors and symptoms of depression.

Measurement of Depression in Patients with Advanced Cancer

According to the *Diagnostic and statistical manual of mental disorders* (2000) fourth edition, text revision, the diagnostic criteria for major depression are the presence of five of nine symptoms that last for at least two weeks. These symptoms are psychological symptoms (depressed mood, anhedonia, worthlessness, suicidal ideation, indecisiveness)

and somatic symptoms (significant weight loss or gain, insomnia or hypersomnia, loss of energy, psychomotor agitation or retardation). The assessment of symptoms of depression among patients with advanced cancer faces several challenges. First, many measures of depression contain items which are not relevant to people with advanced disease (Endicott, 1984). Patients with advanced cancer and near the end of life are likely to obtain high scores on these items even if they are not depressed. Second, somatic symptoms of depression may be due to the disease itself, rather than being indicative of mental illness (Block, 2005; Crawford & Robinson, 2008). Third, most measures of depression that have been validated for use with patients who are ill are too lengthy for use with patients with advanced disease. For example, one of the briefest of these, the *Hospital Anxiety and Depression Scale* (Zigmond & Snaith, 1983) which contains only 14 items, was unable to be completed by 13% of hospice patients (Urch, Chamberlain & Field, 1998). In contrast, Chochinov (1997) found that asking just two questions that assessed the key symptoms of depression, depressed affect and anhedonia, were highly accurate in detecting the presence of depression in patients with advanced disease. Therefore, in this thesis, symptoms of depression were measured using these two questions.

In summary, pain is a challenge to adjustment for many patients with advanced cancer. This thesis explores three dimensions of adjustment (level of coping, quality of life and symptoms of depression) and several potential predictors of adjustment among patients with advanced cancer by using brief instruments to minimise patient burden.

Factors that influence adjustment to pain

Despite wide acceptance of a multidimensional model of pain (e.g., McGrath, 1999; Turk & Melzack, 2001; Woodruff, 1999), most pain research focuses only on pain characteristics (i.e., intensity, frequency, duration) (e.g., Tavoli et al., 2008). Although the relationships between pain characteristics, psychological and social factors have been examined in previous palliative care research, this has usually occurred in the context of investigating barriers to effective pain management (e.g., Ashley, Olimpio, McPherson, Panchal & Passik, 2009; Edrington et al., 2009; Fine, Davies, & Fishman, 2008; Green, Montague & Hart-Johnson, 2009; Portenoy, 1999). Greater awareness of and attention to psychological and social factors may assist in identifying factors other than pain characteristics, that may be amenable to intervention and may help to support positive adjustment. This thesis examines the relationships between cancer pain characteristics, other symptoms, psychological factors and adjustment, to identify the factors that place cancer patients at risk of poor adjustment.

Pain Characteristics in Cancer

The relationship between the presence of pain and patient adjustment has been well documented (e.g., Anderson, Syrjala & Cleeland, 2001, de Wit, van Dam, Hanneman, Zandbelt et al., 1999; Fine et al., 2008; Green, Zwaal, Beals, Fitzgerald et al., 2010; Turk, Sist, Okifuji, Miner et al., 1998). Although the presence/absence of pain is reported in this thesis, the main focus is on the relationship between three characteristics of pain (frequency, duration and intensity) and adjustment.

Cancer patients often report frequent, severe and long lasting pain. In one study conducted in the USA, 92.7% of cancer patients reported pain. This pain was longstanding (average 10.5 months) and often severe in intensity (Caraceni & Portenoy, 1999). Pain in cancer does not appear to be restricted to patients receiving care in a particular health system. A study of cancer patients in Europe and Israel found that 56% of patients reported moderate to severe pain at least monthly (Breivik, Cherny, de Conno, Filbert et al., 2009). Although the prevalence of pain among patients with cancer is high, and there is general acceptance that pain adversely affects adjustment, comparatively little research pertains to the influence of pain intensity, duration and frequency on adjustment. Instead, the focus has been predominantly on the efficacy of various pain medications for reducing pain intensity and not on its influence on adjustment (e.g., Berry et al., 2006; Coyle, 2009; Coyle, Adelhardt, Foley, & Portenoy, 1990; Zeppetella, 2008; Zerzan, Benton, Linnebur, O'Bryant & Kutner, 2010). However, there were a few exceptions, most of which only examined the influence of one pain characteristic (intensity) on various aspects of adjustment. Pain intensity has been associated with poor quality of life (Hwang, Chang & Kasimis, 2002; Jensen, Chang, Lai, Montague & Green, 2009; Mess, Kempinska & Kryzanowski, 2005; Rustoen, Moum, Padilla, Paul & Miaskowski, 2005; Yan & Kin-Fong, 2006), poorer coping (Barkwell, 1991; Elander & Robinson, 2008; Green, Montague & Hart-Johnson, 2009; Lin, 1998; Roberts, Lepore & Helgeson, 2006; Schaeffer & Moos, 1992; Turk et al., 1998), and more symptoms of depression (Barkwell, 1991; Edrington et al., 2010; Fischer, Villines, Kim, Epstein & Wilkie, 2010; Green et al., 2009; Laird, Boyd, Calvin, & Fallon, 2009; McMillan, Tofthagen & Morgan, 2008; Portenoy, Payne & Jacobsen,

1999). On the other hand, only three studies which explored relationships between pain frequency, duration, and adjustment, were identified. In these few exceptions, higher pain frequency was associated with poor quality of life (Rummans et al., 1998; Zeppetella, in press), and more symptoms of depression (Portenoy et al., 1999), and longer pain duration was associated with poor quality of life (Rustoen, Moum, Padilla, Paul & Miaskowski, 2005). Pain frequency and duration may be important to other aspects of adjustment and yet these relationships have not been explored. This thesis therefore proposed to extend existing knowledge about the influence of pain characteristics (frequency, duration and intensity) on adjustment among patients with advanced cancer.

Breakthrough pain. This thesis places particular emphasis on one type of pain, breakthrough pain. Breakthrough pain is defined as a transitory exacerbation of pain that occurs in addition to otherwise stable pain (Portenoy & Hagen, 1990; Mercadante et al., 2002). This thesis has adopted this definition, but also includes transitory pain episodes occurring in the absence of other pain. Breakthrough pain is a commonly reported symptom of cancer, particularly among patients with advanced disease. However, reports about the prevalence, intensity, frequency and duration of breakthrough pain among cancer patients are varied (Table 1.2). There are four main reasons for this variability. First, although the most commonly accepted definition of breakthrough pain is that proposed by Portenoy and Hagen (1990), this has not been adopted universally. As a result, some studies exclude types of pain that were included in other studies. Second, variability may be an artifact of the use of different assessment

tools, or different methods of measurement. For example, when pain duration is recorded, the measure is sometimes from onset to highest intensity (e.g., Hagen et al., 2008; Portenoy et al., 1999; Zeppetella, O'Doherty & Collins, 2000), or from time medication was taken until relief (Hagen et al., 2008; Zeppetella, 2008), rather than the total duration of the pain (Hagen et al., 2008; Rustoen et al., 2005). Third, cancer patients in different studies are often in different stages of disease. The evidence suggests that patients with advanced disease experience more breakthrough pain than patients with less advanced disease (e.g., Colleau, 2004). Fourth, variability in breakthrough pain characteristics may reflect historical and cross-national differences in pain management practices. However, despite the medical innovations in care during the past 20 years, there is little evidence to suggest that breakthrough pain frequency, duration and intensity have significantly declined (Bhatnagar, Upadhyay, & Mishra, 2010; Davies, Vriens, Kennett & McTaggart, 2008; Portenoy & Hagen, 1990; Portenoy, Payne & Jacobsen, 1999; Zeppetella, 2008, in press; Zeppetella, O'Doherty & Collins, 2000). Breakthrough pain appears to be as much of a concern in 2010 as it was in 1990.

Table 1.2

Median Frequency, Duration and Intensity of Breakthrough Pain

Citation	Frequency (per day)		Duration (minutes)		Intensity	
	M	Range	M	Range	M	Range
Portenoy & Hagen (1990)	4	1-36	30	1-240	severe	-
Portenoy et al. (1999)	6	1-60	3	1-30	-	-
Zeppetella et al. (2000)	7	1-14	<30	-	-	severe to excruciating
Davies et. al. (2008)	2	1-10	30	5-360	moderate	mild to severe
Zeppetella (2008)	4	1-8	35	5-75	moderate	mild to excruciating
Bhatnagar et al. (2010)	3.85	1-5	>30	-	severe	-

Measuring Pain in Cancer.

Pain has been assessed in many ways in efforts to understand its relationship to adjustment and to inform treatment. However, this variation in method of assessment has made it difficult to compare the results across studies (Green et al., 2010; Hjermstad, Gibbins, Haugen, Caraceni, Loge & Kassa, 2008; Zeppetella, in press). Methods of assessment also differ across pain characteristics. For example, pain intensity is most commonly assessed using verbal rating scales (VRS), visual analogue scales (VAS) or graphic scales of intensity, and pain location is usually assessed with a pain drawing. Because verbal rating, numerical rating and visual analogue scales have been found to be equally suitable for use among patients with acute and chronic pain, this thesis has assessed pain characteristics using both verbal and numerical rating scales (Cork, Elsharydah, Zavisca, & Alexander, 2004; Holgate, Asher & Thompson, 2003).

Although pain intensity is the most frequently reported characteristic, there are many other characteristics. Frequency, duration, location, temporal, quality, precipitating factors, relation to analgesia, interference, predictability, pathophysiology, aetiology and palliative factors are also reported in some studies (Caraceni & Portenoy, 1999; Fine & Busch, 1998; Fine, Davies and Fishman, 2008; Haugen, Hjermstad, Hagen, Caraceni & Kaasa, 2; Hjermstad et al., 2008; Zeppetella, in press). All these characteristics may be important considerations for treatment and may potentially influence adjustment, however, three characteristics (frequency, duration and intensity) were associated with at least one aspect of adjustment (e.g., Barkwell, 1991; Rummans et al., 1998; Rustoen et al., 2005; Zeppetella, in press). Therefore, this thesis focuses on these pain characteristics.

There is a wide range of pain assessment tools available, but none are universally accepted (Green et al., 2010; Hjermstad et al, 2008; Zeppetella, in press). A comparison of 11 measures found that only two measures had been extensively validated or cross-culturally tested and none had been tested among patients in the last days of life or who are very sick (Hjermstad et al., 2008). Some tools assess only one characteristic (e.g., *Pain Intensity Scale* (Lai, 2003)). In contrast, others are multidimensional. The most widely used multidimensional pain assessment tool among cancer patients is the *Multidimensional Pain Questionnaire* (MPQ) (Melzack, 1975) and the *Brief Pain Inventory* (BPI) (Cleeland, 1991). The MPQ and the BPI are comprehensive, but they do not measure two pain characteristics that may be important in both clinical and research contexts: duration and frequency of episodes of pain. One of the only truly

comprehensive assessment tools is the *Alberta Breakthrough Pain Assessment Tool for Cancer Patients* (Hagen et al., 2008). It encompasses frequency, duration, intensity, location, quality temporal aspects and also qualitative descriptors of pain and includes reports by both patients and clinicians. However its length (15 questions to be completed by the patient for each pain) is too burdensome for most patients with advanced disease. Pain diaries are recommended by many clinicians, but compliance among patients with advanced cancer is limited, particularly when pain is severe (de Wit et al., 1999). Because this thesis explores adjustment to pain among patients with advanced disease, assessment tools need to be as brief as possible, and therefore cannot include all characteristics of pain. This thesis focuses on three pain characteristics (frequency, duration and intensity).

Other Symptoms

Cancer patients often report the presence of multiple symptoms in addition to pain (Coyle, Adelhardt, Foley & Portenoy, 1990; Glare, Krech & Walsh, 1991; Lidstone et al., 2003; Potter, Hami, Bryan & Quigley, 2003; Strömgren et al., 2006; Walling et al., 2010; Wilson et al., 2009). More than 46 symptoms have been reported, including, but not limited to, nausea, vomiting, dry mouth, dyspnoea, constipation, fatigue, fever and loss of appetite. On average, patients reported seven (Potter et al., 2003) to nine symptoms (Lidstone et al., 2003) in addition to pain. These symptoms are often of moderate to severe intensity and often have a high prevalence, but this prevalence and the range of symptoms varies widely. There are three possible explanations for this. First, the studies included patients at different stages in the trajectory of illness. More

symptoms of higher severity are likely to occur in patients with advanced cancer (Potter et al., 2003). Second, the presence and severity of symptoms were assessed differently. Most used checklists containing 21 to 31 options (Lidstone et al., 2003, Potter et al., 2003; Ströngren et al., 2006; Wilson et al., 2009). One of these lists contained only five physical symptoms (in addition to pain) (Wilson et al., 2009). In contrast, in another study, patients were asked to list any additional symptoms, which increased the number of symptoms reported to 46 (Ströngren et al., 2006). Third, the presence and severity of symptoms may be influenced by differences in cancer treatments. For example, in countries where opiates are more readily available, common side effects associated with that medication (e.g., constipation) may be more commonly reported.

Despite general acceptance in the literature that these symptoms have an impact on patients' adjustment, there have been very few studies which have examined these relationships. In two of the exceptions, the presence and severity of non-pain symptoms (fatigue, loss of appetite, constipation, dry mouth) (van den Beuken-van Everdingen, de Rijke, Kessels, Schouten, van Kleef & Patijn, 2009), and dsypnoea (Hench, Bergman, Gustafsson & Gaston-Johansson, 2007), have been showed to be associated with lower quality of life. The first study in this thesis examines the relationships between pain, other symptoms and two aspects of adjustment.

Psychological Factors

Although the intensity of other symptoms is explored in this thesis, it is the influence of psychological factors and pain characteristics and adjustment that is the main focus. A

range of psychological factors may exacerbate or minimise perceived pain and adjustment. Psychological factors which have been reported to be associated with adjustment include positive and negative emotions (Miaskowski et. al., 1997; Syrjala & Chapko, 1995), social support (Chapelle et al., 2008; Gauthier et al., 2009; Miaskowski, 2005; Turk et al., 1998), patient behaviours (e.g., Ahles et. al., 1983; Merluzzi et al., 2001; Turk et al., 1998), beliefs (e.g., Coyle, 2009; de Wit et al., 2001; Flor et al., 1993; Jensen et al., 1999; Richer & Ezer, 2000; Tavoli et. al., 2009), spiritual matters (e.g., Alcorn et al., 2010; Fife, 1995, 2005; Holland et al., 1998, 1999; Strang, 1997), meaning of pain and illness (e.g., Hass-Cohen & Clyde-Findlay, 2009; Park, 2010; Richer & Ezer, 2000) and coping strategies (Miaskowski, 2005; Turk et al., 1998). Although a range of psychological factors have been examined in the context of adjustment in the general population (e.g., Nezu et al., 2007; Parle, Jones & Maguire, 1996), the influence of emotions, and meaning, have been of particular interest among patients with cancer (e.g., Barkwell, 1991; Fife, 2005; Park, 2010). Therefore this thesis proposes to extend previous research by exploring four psychological factors in relation to adjustment (negative emotion, positive emotions, meaning of pain and perceived effectiveness of pain management strategies).

Positive and Negative Emotions

Previous research suggests that emotions influence adjustment in the general population. For example, positive emotions, such as hope, happiness, optimism have been associated with higher levels of adjustment (e.g., Folkman, 1997; Folkman & Moskowitz, 2000; Fredrickson, 2003; Strand, Zautra, Thoresen, Odegard, Uhlig, &

Finset, 2006; Weiten, Lloyd, Dunn & Hammer, 2009). In contrast, negative emotions, such as hopelessness, mood disturbance, loneliness and anger are associated with poorer adjustment (e.g., Gabriel, Jensen, Thornby & Sloan, 2008; Harris, 2003; Lumley, Kelley & Leisen, 1997; McParland, Molton et al., 2009; Whyte & Murphy-Black, 2005).

Negative and positive emotions have also been found to influence adjustment among patients with cancer. For example, “hope” was associated with better adjustment (less psychosocial interference) among newly diagnosed cancer patients (Utne, Miaskowski, Bjordal, Paul & Rustoen, 2008). Similarly, “optimism” was found to be associated with higher quality of life (Wong & Fielding, 2007). In contrast, negative emotions were associated with poorer quality of life (e.g., Lehto, Ojansen & Kellumpu, 2004) and more symptoms of depression (Sist, Florio, Miner, Lema & Zevon, 1998). However, despite the abundance of literature reporting relationships between negative and positive emotions and adjustment, relatively little research on these has been conducted among patients with advanced disease. In two of the exceptions, associations between higher mood disturbance and poorer adjustment have been reported among heterogeneous cancer patients with advanced disease (Knudsen et al., in press; Rummans et al., 2006) and among women with advanced breast cancer (Koopman, Hermanson, Diamond, Angell & Spiegel, 1998). These results provide some evidence that the relationships found between emotions and adjustment in other populations may be generalisable to patients with advanced disease. This thesis explores the relationships between negative and positive emotion and two aspects of adjustment (quality of life and coping) among patients with advanced disease.

Meaning of pain

One psychological factor of particular interest in relation to adjustment to adverse events, illness and pain, is meaning. Although there has been a lot of research exploring meaning, both its conceptualisation and operationalisation in research, and the resulting research findings have been diverse. Many fail to define meaning. For example, they have reported relationships between adjustment and meaning of cancer (e.g., Gotay, 1985), meaning of pain (e.g., Hass-Cohen, 2009) meaning of cancer pain (e.g., Smith, Gracely & Safer, 1998), but did not define meaning. Those who have attempted to define meaning have based their conceptualisation of meaning on Lazarus and Folkman's (1984) coping and appraisal theory (e.g., Chen, 1995; Folkman & Mosowitz, 2000; Lepore & Helgeson, 1998; Richer & Ezer, 2000; Park, Edmondson, Fenster, & Blank, 2008; Weir, Browne, Roberts, Tunks, & Gafni, 1994). These researchers define meaning as a secondary appraisal of an event. Despite the common origin of this set of definitions, the resulting conceptualisations of meaning are diverse. For example, meaning-making was described as intrusive thoughts (Christie, Meyerowitz, Giedzinska-Simons, Gross & Angus, 2009; Lepore & Helgeson; 1998; Salsman, Segerstrom, Brechting, Carlson & Andrykowski, 2009). In contrast, other scholars emphasised a positive reframing of an event. For example, Park et al. (2008) conceptualised meaning as posttraumatic growth, meaning in life and reduced just-world violations.

Other researchers have based their conceptualisation of meaning on a symbolic interactionist approach (Blumer, 1969). This approach is based on three premises:

people act on the basis of the meaning events have for them, meaning arises out of social interaction, and meanings are subsequently modified through an interpretative process (Barkwell, 1991; Caress, Luker, & Owens, 2008; Ferrell & Dean, 1995, Fife, 1995; Liposwki, 1970). Again, despite this common basis, their conceptualisations of meaning are diverse. For example, meaning of illness (e.g., Caress et al., 2008; Liposwki, 1970) and meaning of pain (Barkwell, 1991) were described as the subjective significance of all disease-related information that impinges upon the patient. These were then reported as eight meaning categories that patients ascribe to illness and cancer pain. In contrast, Fife (1995) described meaning of cancer as the patient's understanding of the implications of the illness for his/her identity and the future. Such a diverse range of conceptualisations of meaning make it difficult to compare the resulting findings. In this thesis, the focus is on the meaning ascribed to pain. It is defined as the patients' understanding of the sense they make of their pain, that is, the personal significance of the pain experienced by patients with advanced cancer and breakthrough pain.

Meaning-making and meaning-made. Another distinction in the meaning literature is between the process of “meaning-making” and the outcome of this process “meaning-made”. The “meaning-making” process is dynamic and continues throughout the life span and intensifies in response to specific negative or unexpected events (Thompson & Janigan, 1988). In contrast, “meaning-made” refers to the products of the meaning-making process (Park, 2010) at a particular point in time: that is, the meanings that are ascribed to an event. This thesis explores the “meaning-made” of pain among

patients with advanced cancer and breakthrough pain. That is, the focus in these studies is on the meaning of, or understanding of, or the sense made of, their experience of pain.

Measuring meaning of pain. The ways in which meaning of cancer pain have been assessed are diverse. For example, some researchers have adopted qualitative methods in which themes or categories of meaning were identified from the analysis of interviews with patients (e.g., Barkwell, 1991; Ferrell & Dean, 1995; Lipowski, 1970). Others have adopted quantitative methods and used multi-item scales (e.g., Chen, 1995; Fife, 2005). There are advantages and disadvantages in both approaches. For example, quantitative methods require the patient to respond to specific items and have no scope to identify other meanings that may be relevant to the patient. On the other hand, quantitative methods may allow statistical analyses that determine how much variance in the outcome of interest is accounted for by meaning. In contrast, qualitative usually provide richer information about the meanings patients ascribed to an event, but do not provide a clear protocol for the relative influence of particular meanings on the outcome of interest. This thesis incorporates studies that adopt both approaches.

Findings concerning meaning of pain. There is extensive literature available on the relationships between adjustment and meaning of illness and pain, and also the general acceptance in the literature of the importance meaning has for adjustment of patients. For example, some researchers have explored the meaning made of chronic back pain (Graham, Lobel, Glass & Lokshina, 2008) and illness (Lipowski, 1970; Caress, 2008; Fife, 1995, 2000). However, very few studies of meaning have been

conducted among cancer patients with pain and even fewer have been conducted in a palliative population. Examples of the exceptions include meaning made of cancer (Dirksen, 1995; Fife, 2005; Gotay, 1985; Lepore & Kernan, 2009) and cancer pain (Barkwell, 1991; Chen, 1995; Chung, 2000; Ferrell & Dean, 1995; Park et al., 2008). The findings are not consistent. For example, some studies have found that the meaning of cancer is unrelated to patient adjustment (e.g., Dirksen, 1995; Gotay, 1985; Lepore & Kernan, 2009; Park et al., 2008), while other studies have shown that meaning of pain is related to better adjustment (Fife, 1995, 2005). Similarly, aversive meanings of cancer pain are associated with poorer adjustment (Barkwell, 1991; Ferrell & Dean, 1995) and non-aversive meanings are associated with better adjustment (Barkwell, 1991). It is currently unclear whether these relationships are different when cancer is being actively treated compared to when it is advanced. The present study is one of only two studies which explore these relationships in patients with advanced cancer. It is the only study which assesses meaning of pain in the context of breakthrough pain.

Only one previous study explored the relationship between the meanings patients ascribe to pain and their adjustment, exclusively among patients with advanced disease (Barkwell, 1991). The meaning “challenge” was associated with higher coping and less symptoms of depression. In contrast, the meanings “enemy” and “punishment” were associated with poorer coping and more symptoms of depression. Further research is required in order to ascertain whether relationships found between pain, meaning of pain and adjustment, were unique to one sample of patients. Therefore, this thesis proposed to extend existing knowledge by exploring meaning of pain and two aspects of

adjustment (level of coping and symptoms of depression) exclusively among patients with advanced cancer.

Perception of Pain Management Effectiveness

Another psychological factor that may be related to adjustment is patient's perception of the effectiveness of pain management strategies (Ahles, Blanchard & Ruckdeschel, 1983; Kemp, Ersek & Turner, 2005; Lewis, 1983; Mess et al., 2005). Numerous strategies are available for the management of cancer pain, including pharmacological (e.g., analgesic, adjuvant, steroidal), surgical, psychological, physiological (e.g., physiotherapy, massage, Transcutaneous Electrical Nerve Stimulation (TENS) and alternative (e.g., naturopathic, homeopathic, art, music) interventions.

Pharmacological interventions for cancer pain have been widely researched (e.g., Berry et al., 2006; Davies, Dickman, Reid, Stevens & Zeppetella, 2009; Hakonsen, Strelec, Campbell, Hudson & Loennechen, 2008; Mitera, Fairchild, DeAngelis, Emmenegger et al., 2010; von Gunten, Fairchild, DeAngelis, Emmenegger, 2010; Yennurajalingham, Dev, Walker, Reddy, & Bruera., 2010; Zepettella, 2008; Zepettella & Ribeiro, 2006; Zerzan et al., 2010). Research has also explored the efficacy of a range of strategies used as supplements to pharmacological interventions for cancer pain (Anderson, Syrjala & Cleeland, 2001; Cepeda, Carr, Lau & Alvarez 2006; Huang, Good & Zausniewski, in press; Kutner et al., 2008; Menefee & Monti, 2005; Robb, Oxberry, Bennett, Johnson & Simpson, 2009; Searle, Bennet, Johnson, Callin & Radford, 2009; Spiegel, 1995; Wallace, Rauck, Thippawong, Khanna & Tudor, 2008). Relatively little research has

been conducted on surgical interventions (Easson & Pisters, 2007; Giorgi & Broggi, 1984), psychological interventions (e.g., Cole, 2003; Kwekkeboom, 1999; Kwekkeboom, Hau, Wanta & Bumpus, 2008), physiological interventions (Minton & Higginson, 2007; Robb, Oxberry, Bennett, Johnson, Simpson & Searle, 2008; Searle, Bennett, Johnson, Callin & Radford, 2008) and alternative therapies (Cepeda et al., 2006; Huang et al., in press; Kutner et al., 2008; Pan, Morrison, Ness, Fugh-Berman, & Leipzig, 2000) for cancer pain. Each of these studies focuses on the efficacy of one or two pain management strategies. However, patients often use a variety of different pharmacological, supplementary, and other methods to manage pain. This thesis explores the patients' perception of the combined effectiveness of their whole repertoire of pain management strategies.

Perceived effectiveness of pain management strategies refers to the patient's opinion about the helpfulness of their range of pain management strategies (Calvin, Becker, Beiring & Grobe, 1999; Chapman, Jamison, Sanders, Lyman & Lynch, 2000; Tse, Pun & Benzie, 2005; Wallace et al., 2008). There is a large body of research pertaining to satisfaction with pain management. However, this construct encompasses the sense of being treated correctly, having a proactive treatment plan in place, and collaboration between patient and primary health care providers in addition to perceived effectiveness of pain management (e.g., Beck, Towsley, Berry, Lindau, Field & Jensen, 2010; Dawson et al., 2002; Hwang Chang, & Kasimis, 2002, Tang, Liu, Lin & Chen, 2010; Ward, Donovan & Max, 1998). Therefore, patients may report dissatisfaction with their pain management, and yet also report it to be effective. In addition, pain management

adequacy is sometimes assessed. However this construct is an index of pain intensity relative to strength of analgesia (Cleeland et al., 1994; de Wit et al., 2001; Martin-Rodriguez, D'Amour, & Leduc, 2008). It does not assess the effectiveness of non-pharmacological pain management strategies. Perceived effectiveness of pain management strategies was therefore considered to be a more relevant construct in this thesis.

Measuring pain management effectiveness.

Pain management

effectiveness and satisfaction have been assessed in several ways. Most use single-item Likert (e.g., Hwang, Chang & Kasimus, 2002) or visual analogue (e.g., Chapman, Jamison, Sanders, Lyman & Lynch, 2000) or verbal rating scale (e.g., Calvin, Becker, Biering & Grobe, 1999) scales. The *Patient Opinion of Pain Management Scale* (Calvin et al., 1999) included an item that assessed perceived effectiveness of pain management. This thesis has adopted this single-item as a means of assessing pain management effectiveness without creating an additional burden on patients with advanced cancer.

Findings concerning meaning of pain management effectiveness.

The

perceived effectiveness of the patient's repertoire of pain management strategies is likely to influence adjustment in cancer patients since it is associated with the perceived intensity of pain and symptoms of depression in patients with pain due to non-malignant disease (e.g., Dawson et al., 2002; Hwang et al., 2002; Kemp, Ersek & Turner, 2005). There is wide acceptance that suboptimal management of cancer pain reduces quality of life for patients (e.g., Breivik et al., 2009; Dawson et al., 2002; Mess, Kempinska &

Kryzanowski, 2005; Szetso & Cheng, 2006). It is therefore surprising that relationships between perceived effectiveness of cancer patients' pain management strategies and their adjustment have not been explored, exclusively in patients with advanced disease, even though many of these patients have reported being dissatisfied with the management of their breakthrough pain (e.g., Bhatnagar et al., 2010). This thesis proposes to address this gap in knowledge by examining the relationship between perceived effectiveness of patient's repertoire of pain management strategies, pain characteristics and adjustment among patients with advanced cancer.

Potential Moderators of Pain, Other Symptoms and Adjustment

Although a range of psychological factors have been examined in relation to pain and adjustment, their potential to moderate this relationship has rarely been examined in patients with cancer. One exception is evidence that social support moderates the relationship between pain and adjustment in patients with advanced cancer (Koopman, Hermanson, Diamond, Angell & Spiegel, 1998). However, a wide range of psychological factors, such as personality and social interaction, have been shown to moderate relationships between pain and adjustment in patients with other diseases such as arthritis (Edwards, Giles, Bingham, Campbell, Haythornwaite & Bathon, 2010). There is very little information about whether psychological factors moderate the relationships between pain characteristics and adjustment in patients with advanced cancer, although past research suggests that this is plausible. This thesis, therefore, proposes to examine whether the four psychological factors (negative emotion, positive

emotion, meaning of pain and perceived effectiveness) on which it focuses, moderate the relationship between pain characteristics and adjustment.

Summary

Despite the general acceptance that psychological factors influence adjustment to pain, most research has been conducted in the context of treatment efficacy (e.g., Berry et al., 2006; Coyle, 2009; Coyle, Adelhardt, Foley, & Portenoy, 1990; Zeppetella, 2008; Zerzan, Benton, Linnebur, O'Bryant & Kutner, 2010), or investigating barriers to effective pain management (e.g., Ashley et al., 2009; Edrington et al., 2009; Fine et al., 2008; Green et al., 2009; Portenoy et al., 1999). Generally, only one pain characteristic (intensity) is explored. Although adjustment has been shown to be influenced by pain characteristics (e.g., Rusteon et al., 2005), other symptoms (e.g., Hensch et al., 2007; van der Beuken-van Everingden et al., 2009) and psychological factors (e.g., Barkwell, 1991; Kemp et al., 2005; Richer & Ezer, 2000; Roberts et al., 2006), these are not usually explored in a single study. This is important because these predictors are likely to present a cumulative burden on the patient's resources. Therefore, this thesis explores the relationships between pain characteristics (frequency, intensity and duration), a range of psychological factors (positive and negative emotion, meaning of pain, perceived pain management effectiveness) and three aspects of adjustment (quality of life, level of coping and symptoms of depression).

In addition, a range of psychological factors have been shown to moderate relationships between pain and adjustment in patients with diseases other than cancer (Edwards et al.,

2010; Newith & De Longis, 2004). Therefore, this thesis also proposes to examine whether the four psychological factors (negative emotion, positive emotion, meaning of pain and perceived effectiveness) on which it focuses, moderate the relationship between pain characteristics and adjustment in patients with advanced cancer. A graphic depiction of these relationships to be assessed in this thesis is provided in Figure 1.2.

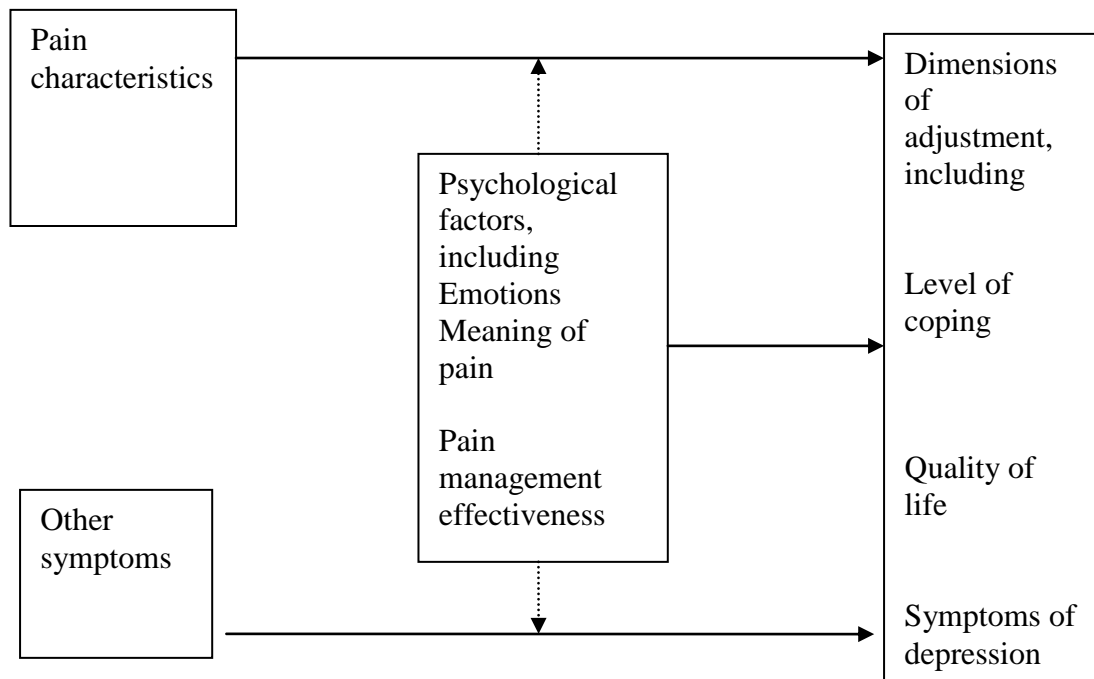


Figure 1.2. Model of the predicted relationships between pain characteristics, psychological factors and adjustment.

Note. This model is an expansion of the model presented earlier (Figure 1.1, p. 25).

Plan for the thesis

This thesis comprises five studies and adopts a mixed methods approach. Study 1 used a large archival data base drawn from multiple palliative care sites in the USA. The study had two aims. First, it explored relationships between the experience of pain, other symptoms, psychological factors and two aspects of adjustment (coping and quality of life). In particular, it examined whether two psychological factors (negative emotions and positive emotions) moderated the relationship between pain characteristics and adjustment. Second, it examined the stability of the relationships between pain characteristics, psychological factors and adjustment by comparing data from the same sample of patients at three different points in time.

Study 2 narrowed the focus to breakthrough pain, a type of pain that may present particular challenges to adjustment for patients with advanced cancer, due to its unpredictability. It also expanded upon the findings of the first study by adding a third pain characteristic (duration) and by exploring whether two other psychological factors (meaning of pain and perceived effectiveness of pain management strategies) were also associated with coping among Australian patients with advanced cancer.

A second sample of cancer patients attending a different Australian palliative care service were recruited for Study 3. This study expanded on the findings of Study 2. Although Study 2 found relationships between meaning of pain and adjustment, these were not the ones that had been predicted. To determine if the findings of Study 2 were artefacts of the choice of measures, Study 3 used different measures of the same

constructs. It also introduced symptoms of depression as an additional measure of adjustment.

The results of Studies 2 and 3 made it clear that most patients reported more than one meaning of pain. In addition, the literature review indicated that there were no clearly defensible quantitative measures of meaning of pain, and therefore qualitative analyses were required to adequately capture the complex relationships between breakthrough pain characteristics, multiple meanings of pain and adjustment. Therefore Study 4 adopted a person-focused qualitative approach that allowed deeper exploration of the meanings ascribed to pain. The meanings revealed in Study 4 were then used in the final study.

The final study was an intensive diary study of a small sample of patients. Study 5 combined the qualitative meaning of pain data derived from Study 4 with quantitative data on breakthrough pain characteristics and adjustment. It explored differences in patterns of breakthrough pain characteristics and adjustment for patients characterised by aversive meanings of pain with those for patients characterised by non-aversive meanings of pain. The final study also examined the day-by-day stability of breakthrough pain characteristics and adjustment.

In summary, this thesis explored relationships between aspects of adjustment, and pain characteristics and psychological factors among patients with advanced cancer. It draws on a large longitudinal archival data-set, small cross-sectional studies and small

prospective case studies. Both quantitative and qualitative, and variable-focused and person-focused approaches were used.