UNIVERSITY OF SOUTHAMPTON

FACULTY OF MEDICINE, HEALTH AND LIFE SCIENCES

School of Medicine

The assessment and management of anxiety and depression in prostate cancer patients being managed with active surveillance.

by

Sam Watts

Thesis for the degree of Doctor of Philosophy

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ABSTRACT

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THE ASSESSMENT AND MANAGEMENT OF ANXIETY AND DEPRESSION IN PROSTATE CANCER PATIENTS BEING MANAGED WITH ACTIVE SURVEILLANCE

By Sam Watts

Over 40,000 new diagnoses of prostate cancer (PCa) were confirmed in 2012 in the UK; the majority localised PCa. Localised PCa does not require radical treatment but can be monitored with active surveillance (AS). AS prevents the risk of over-treatment and the debilitating physical side effects that can accompany it. Very little is known about the psychological ramifications of this management approachh; research suggests AS may increase anxiety and depression. Anxiety is a significant predictor in determining which AS patients will transfer to clinically unnecessary radical treatment. The aim of this thesis was to generate a more definitive estimate of the prevalence of anxiety and depression in AS and to then determine the best ways of supporting these men to allow them to better manage their distress and so avoid unnecessary surgery. Four investigations were undertaken:

Study 1: Systematic Review and Meta-Analysis of Depression and Anxiety in Prostate Cancer. The published literature was systematically searched for studies that recorded the prevalence of depression and anxiety in PCa. 27 articles were identified resulting in a pooled sample size of 4494 patients. The results revealed a high prevalence of depression and anxiety that ranged from 14% to 27%, respectively (CI's: 11.9%-30.1%).

Study 2: A Cross-Sectional Assessment of Depression and Anxiety Prevalence. AS patients were recruited into a large multi-centre, cross-sectional survey involving 7 NHS trusts using postal questionnaires to evaluate depression and anxiety. Across a cohort of 313 AS patients, mean anxiety and depression scores were at 4.84 (SD 3.791) and 3.269 (SD 3.569) with caseness (HADS ≥8) of anxiety at 23% (n=73) and depression at 12.49% (n=39).

Study 3: A Feasibility Study into the Use of Mindfulness Based Stress Reduction in the Management of Depression and Anxiety in Active Surveillance Patients. This study attempted to offer a standardised Mindfulness Based Stress Reduction programme to a group of AS patients. 49 AS patients were approached for recruitment into the study but I was unable to recruit a single patient to trial.

Study 4: A Qualitative Feasibility Study into the Design of a Support Intervention for Managing Distress in Active Surveillance. 20 patients were qualitatively interviewed to determine the key problems and concerns commonly experienced as a result of AS and how best to design support interventions to address them. The findings indicated a need for brief support groups and an AS specific psycho-educational and informational website.

Collectively these investigations have observed that AS patients experience a high prevalence of psychological distress that requires interventional support. The findings also suggest that designing such interventions will require an approach tailored specifically to AS rather than the use of generic modalities such as standardised mindfulness based approaches. This research has important implications for those working within the field of PCa and AS.

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DECLARATION OF AUTHORSHIP

I, Sam Watts declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

THE ASSESSMENT AND MANAGEMENT OF ANXIETY AND DEPRESSION IN PROSTATE CANCER PATIENTS BEING MANAGED WITH ACTIVE SURVEILLANCE

I confirm that:

1. This work was done wholly or mainly while in candidature for a research degree at this University;
2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
3. Where I have consulted the published work of others, this is always clearly attributed;
4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
5. I have acknowledged all main sources of help;
6. Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
7. Part of this work has been published as:

   Watts, S., Leydon, G., Brich, B., Prescott, P., Lai, L., Powell, C. & Lewith, G. (2013). Depression and anxiety in prostate cancer: a systematic review and meta-analysis of prevalence rates. British Medical Journal Open 2014;4: e003901. doi:10.1136/ bmjopen-2013-003901

Signed: .....

Date:.....

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Without the help, assistance and support of many good people, the work making up this PhD would never have reached fruition:

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I am also deeply indebted to the National Institute of Health Research's School of Primary Care for go generously funding the work making up this PhD and the subsequent work that has developed from it. Ultimately, without their financial support all of the ideas that led me onto this path would have remained just that.

On that note I am also deeply grateful to my parents whose constant support, both financial and otherwise, has allowed me to get to where I want to be. Without them I would have failed to get to the start line, let alone the finish line.

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My biggest thank you however is reserved for Professor George Lewith. In so kindly and positively responding to my initial unsolicited email, he guided and set into motion the whole process of events that led from a vague concept to a concrete protocol to subsequent funding and final completion. Professionally he has been untiring in his support and has guided, encouraged, motivated and educated me across the duration of this journey. Personally he has become a trusted adviser and friend on many different levels over the last few years and for that I owe a true debt of gratitude.

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Chapter 1

Introduction and Background

1.1 Prostate Cancer Incidence

Prostate cancer (PCa) represents the most common form of non-cutaneous malignancy diagnosed in British men (Office for National Statistics, 2010). Over 36,000 new cases were diagnosed in 2010, accounting for almost 25% of the total number of male cancer diagnoses that year (Office for National Statistics, 2010). It is estimated that by 2020, PCa will become the most common form of cancer diagnosed in Britain (Ferlay et al., 2010). World-wide, over 913,000 men were diagnosed with PCa in 2008, with two thirds of these men living in developed countries (Ferlay et al., 2010). PCa currently represents the most common form of male specific cancer diagnosed in the USA, Australia, New Zealand and most of Western Europe (Ferlay et al., 2010).

Over the last three decades, PCa incidence rates within the UK have trebled from 33 cases per 100,000 men in 1975 to 97 cases per 100,000 men in 1997 (Office for National Statistics, 2010). This pattern shows no sign of abating. The most recent statistics, monitored over the previous decade (1998-2008), reveal a 49% increase in confirmed PCa diagnoses in England alone (Cancer Research UK, 2010). Similar patterns exist in the majority of the Western World, the most dramatic of which have occurred within the USA which has seen an 82% increase in PCa incidence since 1986 (Potosky et al., 1995).

In the most part, this increase is due to the advent of the Prostate Specific Antigen (PSA) test (Melia et al., 2004). The PSA test provides a fast and economically viable method of screening men for the presence of potential PCa via a single blood test. In many countries, including America, PSA screening is offered as standard protocol to all men aged over 50 (American Cancer Society, 2010). However, the use of PSA screening remains controversial and is not offered within the current NHS framework. This is primarily due to the lack of conclusive evidence suggesting that the diagnosis of early, localised PCa in asymptomatic men is beneficial to either their survival or their subsequent quality of life (Etzioni et al, 2002). Despite this, the number of men undergoing PSA screening in the UK, both privately and within the NHS, continues to rise (Oliver, Gunnell & Donovan, 2000).

Additionally, PCa incidence is significantly correlated to age. For younger men aged 55-59, the incidence rate is as few as 151 men per 100,000. However, this increases to 515 cases per 100,000 for men aged 65-69 and jumps to over 744 cases per 100,000 for men aged 85 years or older (Office for National Statistics, 2010). Due to increased standards of living and wider access to medical care, men in the Developed World are currently living for significantly longer than their predecessors (Office for National Statistics, 2010). Given that PCa incidence increases significantly with age, this increased longevity has been highlighted as a key contributory factor in the increased incidence of PCa within the Developed World (Burford, Kirby & Austoker, 2008; Office for National Statistics, 2010). In light of our aging population, coupled with the increased use of PSA screening, the annual incidence of PCa within the UK and most of the Developed World is predicted to significantly increase year on year over the next decade (Office for National Statistics, 2010).

2.1. Localised prostate cancer: A burgeoning health problem

In almost all cancer sites other than PCa, a confirmed diagnosis will result in the immediate implementation of radical treatment. Such treatment can take many forms, including surgery, chemotherapy, radiotherapy, hormone therapy and immunotherapy. For men diagnosed with locally advanced, advanced or metastatic PCa, the same is also true. Such men are offered and recommended immediate radical intervention with curative, life prolonging or palliative intent. In these instances, the recommended treatment pathways for PCa are very clearly defined by the recently updated National Institute for Clinical Excellence (NICE) Clinical Guidelines and include surgery, radiotherapy and hormone therapy (NICE, 2014).

However, of the 36,000 new cases of PCa diagnosed in the UK each year, the majority will be diagnosed with slow growing, localised PCa (Cancer Research UK, 2010). Men diagnosed with localised PCa usually present with a mild symptom burden, such as urinary dysfunction, or are increasingly asymptomatic and are diagnosed through routine blood tests (Pickles et al., 2007). For such men, treatment selection can be a far more ambivalent and distressing process.

Research suggests that during the cancer treatment decision making process, patients intuitively desire radical treatment as they associate this with an increased chance of long term survival (Klotz, 2013). However, for men diagnosed with localised, non-invasive PCa, (Gleason score <7; PSA <10), current clinical guidelines recommend that such men be offered non-invasive management with regular clinical assessments (NICE 2014) with surgery and radio

therapy available for those who would prefer radical intervention. This management approach is called active surveillance (AS)

1.3. Active Surveillance for the management of localised prostate cancer

AS involves the systematic monitoring of men with localised, non-aggressive PCa with routine biopsies, PSA tests and MRI utilising the following recently updated NICE clinical guidelines:

Timing	**Tests**
At enrolment in active surveillance	Multiparametric MRI if not previously performed
Year 1 of active surveillance	Every 3-4 months: measure PSA (prostate-specific antigen) Throughout active surveillance: monitor PSA kinetics Every 6-12 months: DRE (digital rectal examination) At 12 months: prostate re-biopsy
Years 2-4 of active surveillance	Every 3-6 months: measure PSA Throughout active surveillance: monitor PSA kinetics Every 6-12 months: DRE
Year 5 and every year thereafter until active surveillance ends	Every 6 months: measure PSA Throughout active surveillance: monitor PSA kinetics Every 12 months: DRE

Table 1: NICE Clinical Guidelines 175 (Reference: National Institute for Clinical Excellence clinical guideline 175. (2014). Prostate Cancer: diagnosis and treatment.

For men whose tumours show clinically significant growth, radical treatment can be immediately implemented. Men whose disease remains stable can remain on AS indefinitely. There are many benefits to AS, both for service users and service providers.

For the former, AS avoids the debilitating physical side effects of radical intervention that commonly include impotence and incontinence (Potosky, Legler & Albertsen, 2002), treatment induced reductions in quality of life and the risk of surgical and post-surgical complications (Bloch et al., 2007; Carlsson et al., 2010). More crucially, a comprehensive prospective

longitudinal investigation conducted in the US has definitively shown that for men with low grade PCa, being managed with observation was not associated with any significant reductions in 12-year survival in comparison to men undertaking radical intervention (Wilt et al., 2012).

It is important to note that several earlier investigations report findings which oppose those observed by Wilt et al, (2012). These suggest that managing localised PCa with AS does reduce PCa specific survival times (Iversen, Madsen, & Corle, 1995; Lu-Yao et al., 2009). However, these differences were minimal and the studies were conducted before the widespread utilisation of routine PSA testing, meaning that study participants were diagnosed symptomatically. Such men were likely to have had more aggressive PCa histology than their asymptomatic counterparts diagnosed via PSA tests. This may account for the poorer survival times observed.

Unfortunately, no additional definitive prospective longitudinal investigations comparing survival among those managed with AS and those treated radically for localised PCa currently exist. The results of the large international Protect T study, comparing survival outcomes between AS and radical treatment, are due in June 2015 (Lane et al., 2014). These will provide a more definitive insight into the effectiveness and survival differences associated with AS.

Utilising AS for the management of localised PCa may also offer economic benefit to service providers. Over-treating men with Gleason 6 PCa who could be managed with AS involves expensive surgical intervention and follow up; performing one radical prostatectomy comes at a cost of £9000 to the NHS (Department of Health, 2012). Each year it is estimated that almost 20% of men diagnosed with slow growing, indolent PCa in the UK opt for radical intervention in the absence of disease progression (NICE, 2009). This suggests that there may be an economic benefit to utilising AS to manage men diagnosed with localised PCa. However, such benefits have yet to be formally investigated and it is important to note that the monitoring procedures inherent to AS, such as biopsies and repeated MRIs, may detract from any such economic gains.

These findings suggest that for clinically suitable men, AS represents the optimal treatment protocol to adopt. However, concerns currently exist regarding the psychological ramifications of this treatment approach (Burnet et al., 2007; Pickles et al., 2007). Evidence exists to suggest that cancer patients undergoing radical treatment feel encouraged, empowered and hopeful through the initiation of radical and potentially curative treatment (Salander, Bergenheim &

Henriksson, 1996; Davidson & Degner, 2007). In many instances this results in an increased sense of optimism and psychological wellbeing. Men being managed with AS do not experience these positive emotions due to the essentially passive nature of AS. It has been suggested that diagnosing a man with PCa and then informing him that no radical treatment is recommended may predispose the patient to a far higher risk of psychological distress (Pickles et al., 2007).

There currently exists a lack of good evidence to support this notion, particularly in the UK. Only one UK based study has aimed to assess the differing levels of psychological distress between men managed with AS in comparison to those managed radically (Burnet et al., 2007). This study found no significant difference in anxiety between men treated with AS and those treated radically. However it is important to note that despite this lack of statistical significance, Burnet et al (2007) identified that PCa patients being managed with AS experienced over twice the prevalence of clinical anxiety as PCa patients being managed radically. The clinical implications of elevated anxiety in AS patients are substantial.

Amongst men being managed with AS, anxiety currently sits as a significant predictor in determining which men will transfer to unnecessary radical intervention. Patel et al., (2004) observed that 12% of PCa patients with localised diseased being managed with AS transferred to radical treatment in the absence of any clinically meaningful signs of disease progression.. Likewise, Latini et al.,(2007) revealed that the rate of change of anxiety was a more significant predictor in identifying which AS patients transferred to radical treatment, and when, than objective clinical markers of disease progression such as rising PSA levels. This would suggest that among AS patients with stable and non-progressive disease, elevated and unmanaged anxiety impacts upon their desire to transfer to clinically unnecessary radical intervention. Whilst not all radically treated PCa patients experience physical side effects, many do with evidence suggesting that between 60%-81% of radically treated patients experience impotence and incontince (Wilt et al., 2012; Potosky et al., 2002)) for no meaningful gain in long term survival (Wilt et al., 2012). In some instances patients may be prepared to accept these side effects, which in some cases are transient, to increase their chances of long term survival (van Tol-Geerdink et al., 2006).

Due to the negative clinical impacts of anxiety on men being managed with AS and its significance in predicting which AS patients will transfer to unnecessary radical treatment, anxiety represented the primary psychological variable of assessment among the AS patients

in the current PhD. However, whilst being a wholly independent condition, depression very often coexists alongside anxiety; as many as 65% of cancer patients with clinical anxiety also experience depression (Bitran, Barlow & Spiegel, 2009). Indeed, the coexistence of depression alongside anxiety is so commonplace that the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-IV) recommends that if a cancer patient is diagnosed with clinical anxiety then the clinical care team should routinely screen for depression (Wise & Rieck, 1993).

Due to this likely coexistence of depression amongst anxious patients, I have also chosen to select depression as my second key psychological variable in this PhD. An additional reason for selecting these two variables was that the small foundation of research that currently exists into the assessment of psychological distress in AS patients has also utilised depression and anxiety as their chosen psychological outcome variables (Steineck et al., 2002; Burnet et al., 2007; van den Bergh et al., 2009; van den Bergh et al., 2010). Thus by choosing to also utilise depression and anxiety in the current PhD, I will be able to directly compare and contrast my findings with those generated by the previously conducted research.

As I will be identifying, measuring and looking at how best to manage anxiety and depression in AS patients over the course of this PhD it was important to provide a theoretical and psychological introduction and overview of these two conditions.

1.4. An introduction and overview of anxiety and depression

1.4.1. Anxiety

Anxiety is a psychological condition associated with feelings of fear, dread, worry, apprehension and a sense of impending disaster (Tyrer & Baldwin, 2006; Bitran et al., 2009). Along with psychological symptoms, anxiety can also present with physical symptoms that commonly include sweating, butterflies, rapid breathing and insomnia (NICE, 2011; Bitran, Barlow & Spiegel, 2009).

Anxiety is broad condition that encompasses a variety of specific anxiety disorders such as panic disorder, agoraphobia, social anxiety disorder, specific anxiety phobias, obsessive-compulsive disorder, post-traumatic stress disorder and Generalised Anxiety Disorder (GAD).

The anxiety experienced by medical patients, including cancer patients, as a result of their diagnosis and treatment falls under the umbrella of GAD (NICE, 2011).

GAD is characterised by persistent feelings of worry, apprehension, restlessness, panic and fear (NICE, 2011) which in many instances may be out of proportion to the threat being faced. The most commonly utilised diagnostic system for GAD is the American Psychiatric Association's (2010) Diagnostic and Statistical Manual (DSM-IV). The characteristic symptoms utilised for diagnosis include:

1. A physical and emotional response that is out of proportion to the level of threat being faced.
2. A persistence of symptoms or deterioration without intervention.
3. A level of symptoms which are unacceptable regardless of the level of threat.
4. A disruption of usual or desirable interaction and functioning.

GAD was first classified as an independent condition in 1987 under the guidelines of the DSM-III criteria (American Psychiatric Association, 1987) and has since become a widely researched and documented independent psychological condition. In the majority of the cancer based research, anxiety disorders are commonly defined simply as "anxiety;" technically this is incorrect (NICE, 2011). The specific type of anxiety that most cancer patients experience as a result of their diagnosis and treatment is GAD (Bitran, Barlow, & Spiegel, 2007). Thus in the current investigation all reference to anxiety will be based upon the concept of GAD rather than any of the other anxiety disorders listed previously.

1.4.2. Causes of anxiety within cancer

In the public mind cancer is a dreaded disease that is associated with pain, suffering and death (Klotz, 2013). Whilst cardiovascular disease kills more people in the Western World than cancer (World Health Organisation, 2013), surveys have found that when individuals are asked what disease they would most strongly choose to avoid, cancer is the unequivocal answer (Chambers et al., 2011). Indeed, such is the anxiety inducing nature of the word cancer that in psychological experiments designed to assess the impact of verbal prompts on anxiety levels, the word cancer was significantly the most anxiety inducing word identified (Bradley et al., 1995). Thus one of the key causes of anxiety in cancer patients is believed to be the general socialital connotations of the disease rather than any specific anxieties relating to treatment and treatment related side effects (Stark & House, 2000).

Whilst radical cancer treatments such as chemotherapy, radiotherapy and surgery have all been shown to induce clinically significant levels of anxiety (Stark & House, 2000), in many instances cancer related anxiety has been shown to be highest in patients not receiving radical treatment. For example, Hughes et al., (1987) identified that patients with advanced lung cancer who were not receiving chemotherapy had significantly higher levels of anxiety than patients with the same diagnosis who were. This anxiety was attributed to the hopelessness associated with doing nothing.

Likewise, in a randomised controlled trial of adjuvant chemotherapy against observation for early stage breast cancer, patients in both arms had equally high levels of anxiety (Cassileth et al., 1996). However, those not receiving chemotherapy were free from the distressing physical side effects of this treatment approach which are often believed to be a predominant cause of anxiety in patients (Stark & House, 2000). This again suggests that the anxiety induced by "doing nothing" was at least equal to the anxiety caused by the physical side effects of intervening radically. Such findings suggest that the levels of anxiety in cancer patients not being radically treated are in some instances equal to or higher than that experienced by patients who are being radically managed.

By definition, AS is a passive management approach to PCa that does not involve radical intervention. Whilst PCa patients opting for AS may avoid the debilitating physical side effects of radical treatment, the passivity of "not treating" the cancer may predispose and induce a higher prevalence of anxiety, as was found by Hughes et al., (1987) and Cassileth et al., (1996) within the realm of lung and breast cancer and by Burnet et al (2007) in a small sample of UK based AS patients.

Furthermore, cancer monitoring procedures such as blood tests, MRI and CT scans and X-rays have all been shown to induce significant hikes in anxiety (Dale et al, 2005). This is due to the medical procedures themselves, the association-anxiety of having to go to hospital which for cancer patients is often a dreaded place (Hickok, Roscoe, & Morrow, 2001) and the anxiety inducing wait for the subsequent test results (Dale et al., 2005; Lofters et al., 2002). Patients being managed with AS routinely receive one or more of these procedures every 3-6 months to monitor disease progression. It is likely that for AS patients, the routine exposure to such procedures is likely to represent another key cause of anxiety (Pickles et al., 2007; Klotz, 2013).

The above highlights that cancer and its management represent many anxiety inducing components. These apply to all cancer sites and stages, not just PCa. However, due to the unique nature of AS, it is possible that men being managed with this approach may be at an increased risk of anxiety due to the passivity associated with AS and the many monitoring procedures inherent to it.

1.4.3. Consequences of anxiety in cancer patients

Elevated anxiety amongst cancer patients is associated with significant reductions in quality of life and psychological and emotional health (NICE, 2011). Cancer patients with anxiety also report higher incidences of physical symptomology. For example, anxious patients express higher levels of fatigue, nausea and vomiting, increased side effects of treatment, a slower transition from secondary to primary care and require more primary care support (Brown & Kroenke, 2009; Hickok, Roscoe, & Morrow, 2001; Cameron, Leventhal & Love, 1998; Stark & House, 2000). Cancer patients who are anxious are also at a significantly greater risk of developing additional psychiatric morbidities such as depression (NICE, 2011).

However, it is difficult to delineate the direction of the causal relationship between anxiety and physical and psychological side effects; it may be that physical side effects increase a patient's predisposition to anxiety rather than anxiety precipitating the increased side effects. There is currently insufficient evidence to conclusively confirm the direction of this relationship. However, several studies exist showing that cancer patients with anxiety who have completed treatment go on to experience an increased incidence of physical side effects for longer than their non-anxious counterparts (Cameron et al., 1998; Mogg et al., 1995), suggesting that, at least in some cases, anxiety is the causal variable.

The presence of anxiety in men being managed with AS is of additional clinical importance and relevance. Anxiety currently acts as a significant predictor in determining which AS patients will transfer to clinically unnecessary radical intervention in the absence of any sign of clinical disease progression. Such men risk the debilitating physical side effects of radical treatment for no increase in 12 year survival (Wilt et al., 2012).

1.4.4. Measuring anxiety in cancer

There are myriad well validated and reliable questionnaires currently available for the quantitative measurement of anxiety. These include the State-Trait Anxiety Inventory, the Clinical Anxiety Scale, the Hamilton Anxiety Scale and the Hospital Anxiety and Depression Scale. As the measurement of anxiety represented a core component of the work making up this PhD, it was fundamental to select a questionnaire that would provide a valid and reliable quantification of anxiety but also one that would allow direct comparison with the previously conducted PCa and AS specific research. A full psychometric assessment of the available questionnaires was beyond the scope of this PhD. However, a comprehensive assessment, overview and rationale for my choice of questionnaire for measuring anxiety is provided in section 2.4 of Chapter 4.

1.4.5. Depression

Depression is a broad and heterogeneous diagnosis that is characterised by a variety of symptoms (NICE, 2009). The central tenets of depression are a depressed and lowered mood state and the near or total loss of pleasure in most or all activities. There are a variety of depression categories which are determined by both the number and severity of symptoms, as well as the degree of functional impairment.

In most cases a diagnosis of depression is made utilising the DSM-IV system which was developed by the American Psychiatric Association and currently represents the “gold standard” form of diagnosis (American Psychiatric Association, 2010). The DSM-IV classification system requires at least five out of nine depressive symptoms for a diagnosis of major depression. Symptoms must be present for at least two weeks and each symptom should be present at sufficient severity for most of every day. The DSM-IV diagnostic system also requires at least one key symptom such as low mood, loss of interest and pleasure or loss of energy to be present.

These diagnostic criteria allow for the clinical identification of a major depressive episode. However, in recent years, particularly within the field of oncology, it has been recognised that individuals presenting with symptoms that fall below those listed by the DSM-IV criteria for major depression can still result in distressing and disabling levels of depression (NICE, 2009). Consequently current NICE clinical guidelines recognise 'sub-threshold depressive symptoms',

which fall below the criteria for major depression as categorised by the DSM-IV but are still of a disabling nature (NICE, 2009). Sub-threshold depression is defined as at least one key symptom of depression but with insufficient other symptoms and/or functional impairment to meet the criteria for full diagnosis.

However, it is important to note that a degree of sub-threshold depression following a cancer diagnosis is relatively common and in many cases dissipates over time without the need for any form of intervention (Chochinov, 2001). It is when sub-threshold depression does not dissipate naturally over time that it becomes an issue of clinical importance. This is primarily due to the negative impact that depression can have upon a patient's quality of life and clinical decision making processes (Chochinov, 2001, Reich, Lesur & Perdrizet-Chevallier, 2008).

The majority of investigations measuring depression in cancer populations have utilised questionnaires such as the Beck Depression Inventory, the General Health Questionnaire, the Hospital Anxiety and Depression Scale, the Montgomery-Asberg Depression Rating Scale and the Hamilton Rating Scale for Depression. The psychometric analyses of the concurrent validity of these questionnaires (against the DSM-IV criteria) have revealed that the strongest correlations exist against symptoms of mild to moderate depression rather than major depression (NICE, 2008). This would suggest that the definition of depression used and measured by a large proportion of the related cancer research refers to the former rather than the latter. Therefore in this thesis depression will refer to the presence of mild to moderate depression rather than a major clinical depressive episode.

1.4.6. Prevalence, causes and consequences of depression in cancer

A large foundation of evidence exists to demonstrate the existence of depression amongst cancer patients (Pasquini & Biondi, 2007). The reported prevalence data suggests that over 50% of cancer patients experience clinical depression at some stage of their cancer journey (Pasquini & Biondi, 2007).

The causal factors responsible for the development of depression among cancer patients tend to fall into two distinct categories; personal and medical. For the former, variables such as coping ability, social support, religious beliefs, personality traits and distance from hospital have all been shown to correlate to depression (Okamura et al., 2002; Pasquini & Biondi, 2007; Bailey et al., 2005). For the latter, cancer site and stage, prognosis, treatments undertaken and

follow up support have been identified as the most important variables associated with the development of depression (Ell et al., 2005; Okamura et al., 2002; Pasquini & Biondi, 2007; Bailey et al., 2005).

In addition to these personal and medical variables, the broader psycho-social connotations of cancer and its treatment have also been shown to be correlated to depression (Pasquini & Biondi, 2007). Receiving a positive diagnosis of cancer is an extremely traumatic experience and one that leaves the patient facing the possibility of death, invasive treatments, on-going side effects, chronic pain, changes to body image and changes to their role in the family, the work place and society at large (Pasquini & Biondi, 2007). All of these issues may predispose cancer patients to a higher risk of depression.

The clinical consequences of depression with the oncological setting are high. Cancer patients experiencing depression have a reduced quality of life (Reich, Lesur & Perdrizet-Chevallier, 2008), require significantly longer periods of hospitalisation (Ashbury et al., 2003), are less likely to comply with their cancer related treatment (Pasquini & Biondi, 2007), experience a greater risk of suicide (Robson et al., 2010) and have higher cancer specific mortality rates (Satin, Linden & Philips, 2009).

Cancer patients with depression also display significantly lower levels of psychological resiliency and coping ability (Walker, Zona, & Fisher 2006; Pasquini & Biondi, 2007). Relating specifically to AS, it has been highlighted that to cope effectively with AS, patients require a high degree of resiliency and strong and effective coping abilities to allow them to manage the passivity and uncertainty associated with AS (Hedestig, Sandman & Widmark, 2003; Pickles et al., 2007). Developing depression may therefore reduce an individual's ability to effectively remain on and cope with the psychological demands of AS. For this reason the identification and management of depression in this patient group is of clinical importance

1.4.7. Measuring depression

The universally accepted and established method of assessing depression in adults is through the American Psychiatric Association's Structured Clinical Interview utilising the Diagnostic and Statistical Manual (DSM-IV) guidelines (American Psychiatric Association, 2010). However, this approach is costly and time consuming to administer and involves the expertise of a suitably qualified and experienced clinician. Consequently a variety of brief questionnaires for the

assessment and screening of depression have been developed, the most commonly utilised of which include the Beck Depression Inventory, the Montgomery-Asberg Depression Rating Scale, the Hamilton Rating Scale for Depression and the Hospital Anxiety and Depression Scale. These have been extensively researched and have all demonstrated high levels of concurrent validity in their ability to screen for and identify possible or probably depression.

As the measurement of depression represented a core component of the work making up this PhD, it was fundamental to select a questionnaire that would provide a valid and reliable quantification of depression but also one that would allow direct comparison with the previously conducted PCa and AS specific research. A comprehensive assessment, overview and rationale for my choice of questionnaire for measuring depression is provided in section 2.4 of Chapter 4.

1.5. Anxiety and depression in active surveillance

The use of AS for the management of localised PCa has only been popularised in the last decade. Consequently there exists a substantial dearth of research into the assessment and impact of depression and anxiety in men living with and being managed by AS. Given the substantial clinical, psychological and economic impact of elevated anxiety among AS patients, this represents a substantial void in our understanding of the management of low grade PCa with AS. Current guidelines predict that by 2020, PCa will become the most prevalent cancer in the UK. The majority of PCa being diagnosed is low grade and indolent and therefore ideally managed with AS. Yet if living with AS predisposes patients to higher levels of psychological distress, which in turn causes patients to transfer to clinically unnecessary radical treatment (Patel et al., 2004; Latini et al., 2007), generating a better understanding of the specific prevalence of psychological distress in this patient cohort should form a fundamental component of any future AS specific research.

The limited foundation of research that has attempted to define depression and anxiety prevalence specifically within AS patients have utilised small sample sizes from single sites (Burnet et al., 2007; van den Bergh et al., 2009; van den Bergh et al., 2010), only one of which was conducted in the UK (Burnet et al., 2007). At present the prevalence of depression and anxiety has yet to be definitely defined from a large sample of AS patients from multiple sites within the UK. Generating such data would allow those working within the realms of AS to become more aware of the likelihood of psychological distress in the patients they treat and if

the prevalence data generated is high, will support the need for the development of interventional support to allow patients to better manage any distress they are experiencing. One potentially fruitful form of interventional support that may be effective at equipping AS patients with the means of effectively self-managing their anxiety and depression is Mindfulness Based Stress Reduction (MBSR).

1.6. The management of depression and anxiety in active surveillance; why MBSR?

MBSR is a psycho-educational support programme, created in the meditative traditions of Buddhism, which aims to empower patients to experience life in a non-judgemental and transient way (Kabat Zin, 1990). MBSR emphasises the importance of accepting all thoughts and experiences as they are, good and bad alike, without trying to alter or change them. In doing so, one learns to live more readily in the present moment (i.e. more mindfully), which in turns allows one to prevent the constant ruminative processes of what may happen in the future.

Across the generic cancer research, a variety of non-mindfulness based psycho-educational approaches for the management of depression and anxiety have been utilised and investigated. These have included Cognitive-Behavioural Therapy, motivational interviewing, Acceptance and Commitment Therapy, psychotherapy, counselling and health coaching (Osborn, Demoncada & Feuerstein, 2006). All of these approaches have shown promising results and could, to a greater or lesser extent, have been chosen as my support intervention of choice in this PhD. However, there exists a variety of reasons why MBSR may be a particularly well suited and effective intervention for managing depression and anxiety specifically within AS.

Firstly, men being managed with AS are either asymptomatic or experiencing a very minor symptom burden (Pickles et al., 2007). They are free from any treatment related side effects and have an extremely good long term prognosis. Therefore in most cases AS patients experience no reduction in physical health and wellbeing from pre-diagnosis to post-diagnosis. Despite this, from the time that their cancer is diagnosed, AS patients routinely experience a marked reduction in health related quality of life (QoL) and psychological and emotional health (Hedestig, Sandman & Widmark, 2003; Pickles et al., 2007).

Research suggests that this reduction in QoL and psychological health is predominantly due to ruminative processes which results in AS patients focusing on what may happen in the future rather than on what is actually happening in the present moment (Hedestig, Sandman, & Widmark, 2003; Kronenwetter et al., 2005). This in turn leads to irrational fears of sudden, aggressive and unchecked disease progression, failing health and death.

One of the key reasons for selecting MBSR as my support intervention of choice in the current PhD was that MBSR teaches individuals how to ground themselves non-judgementally in the present moment. By learning mindfulness it was hypothesised that AS patients would be able to more objectively identify with the indolent and non-aggressive nature of their cancer and see that the causes of their distress are due to cognitive ruminations about what may happen in the future and not about what was actually happening in the present moment and see rather that their prognosis was very good. In this way AS patients, thought being more mindful of the objective facts of their diagnosis and treatment, instead of focusing on their irrational subjective fears, would be better placed to cope with the inherent uncertainty associated with AS and so by reduce any anxiety or depression they were experiencing.

Secondly, MBSR was designed to be run in a group setting typically made up of between 10-20 individuals (Kabat-Zinn, 1990). Across the cancer related research, investigations trialling MBSR have tended to utilise a group size of between 10-15 (Dobkin, 2008; Carlson et al., 2007; Lengacher et al., 2010) cancer patients. If interventions that are effective at managing psychological distress in AS patients are to become embedded into the NHS as a part of the routine care package, they will have to be not only clinically effective but also economically viable and sustainable. For example, CBT and counselling may offer a clinically effective approach for managing depression and anxiety but these require costly private one on one consultations which at the moment the National Health Service cannot afford given that it is currently disbanding adjuvant psychological services in many Trust locations across the UK (Parsonage & Naylor, 2012).

In contrast one standardised MBSR programme could be offered to between 10-15 AS patients. This would substantially reduce any associated costs such as practitioner fees and room hire charges and consequently offer excellent value for money. Therefore if MBSR can be shown to be effective at lowering depression and anxiety in AS patients, as it has for other cancer sites, it would offer a clinically and economically viable intervention to allow AS patients to self-manage their distress in a form that may be possible to embed and integrate

into the NHS in a way that other more cost and time demanding interventions such as CBT and counselling cannot.

1.7. Research Aims

The primary aim of the current PhD was firstly to more definitively quantify the prevalence of anxiety and depression in a large sample of AS patients in the UK and secondly to determine how best to support these patients to allow them to better manage any anxiety and depression they are experiencing.

Within these general aims existed more specific research questions. For the sake of clarity, the following provides an overview of each chapter making up this PhD and highlights the research aims and objectives inherent to each:

Chapter 2: A narrative literature review of depression and anxiety in prostate cancer.
The aim of this chapter was to provide an initial overview and critical appraisal of the literature pertaining to the prevalence of depression and anxiety in generic PCa. This would allow me to determine whether enough research evidence existed to allow for the running of a systematic review and meta-analysis into the prevalence of depression and anxiety in PCa. It was also the aim of the literature review to identify and provide an initial insight into the foundation of research into depression and anxiety specifically within patients being managed with AS.

Chapter 3: Depression and anxiety in prostate cancer: a systematic review and meta-analyses of prevalence rates.
The aim of this chapter was to rigorously and systematically identify and review the available research to provide the first meta-analysis of depression and anxiety prevalence rates within PCa across the treatment spectrum. Whilst the overriding aim of this PhD was the assessment and management of depression and anxiety specifically within AS, by firstly understanding how prevalent psychological distress was across the full spectrum of PCa treatments, I would be better placed to determine how the prevalence rates obtained specifically for AS compared against those observed for generic PCa. It was also the aim of the this systematic review was to extract all data relevant to AS patients that may have been reported within studies that evaluated PCa as a whole and thus may not have been identified in my narrative review chapter (Chapter 2).

Chapter 4: A quantitative cross-sectional analysis of the prevalence of clinical depression and anxiety in prostate cancer patients undergoing active surveillance.

Having provided an initial estimate of depression and anxiety prevalence across the PCa treatment spectrum in Chapter 3, the aim of this chapter was to more definitively define the percentage prevalence of clinically meaningful depression and anxiety specifically in PCa patients being managed with AS with a large cross-sectional questionnaire survey. It was my aim to open recruitment centres in multiple locations across the UK and recruit a large sample of AS patients to help increase the generalisibility and representativeness of the generated results. I also wanted to collect a variety of patient demographic data to allow me to determine if any of these demographic variables were significantly associated with depression and anxiety prevalence. Lastly, a distinct paucity of research into the psychological health of Afro-Caribbean PCa patients currently exists. Given that men from this ethnicity are at a greater risk of developing PCa (Ben-Shlomo et al., 2008), I wanted to open recruitment centres in geographical locations with a higher percentage of Afro-Caribbean men to maximise my chances of recruiting men of this ethnicity into the investigation.

Chapter 5: A narrative literature review of supportive psychological interventions within prostate cancer.

Having generated a more definitive estimate of depression and anxiety prevalence amongst AS patients in Chapter 4 and highlighted the need for the better management of these conditions, the aim of this chapter was to overview the literature regarding the kinds of supportive psychological interventions that have previously been trialled amongst PCa patients. Whilst it was my aim to focus wherever possible on interventions designed specifically for AS patients, the paucity of research within this area meant that it was necessary to include interventions designed for PCa across the treatment spectrum. The aim of this chapter was to allow me to better understand whether in men with PCa, do psychological, emotional, informational and cognitive interventions improve psychological health and wellbeing and are PCa patients willing to recruit into such interventions. This information would help me to determine what kinds of interventions would and would not work within the realm of PCa and thus be better placed to determine whether a group based mindfulness based intervention (MBSR) would be a suitable intervention to trial.

Chapter 6: A feasibility and qualitative evaluation of MBSR in the management of depression and anxiety in prostate cancer patients undergoing active surveillance.

Having determined in Chapter 5 that based upon the available research, MBSR was a suitable intervention to trial, the aim of this chapter was to determine the feasibility and effectiveness of MBSR as a tool to allow AS patients to self-manage their depression and anxiety. Utilising a mixed methods approach would allow for both the quantitative assessment of the effectiveness of MBSR in the management of depression and anxiety whilst also allowing for the qualitative assessment of how AS patients found the experience of MBSR and in what ways the standard programme could be modified to make it more appealing and relevant to AS patients. This investigation would allow me to determine AS patients willingness to recruit into an MBSR intervention and what the subsequent adherence rates would be and ultimately how effective MBSR was as a tool to lower depression and anxiety.

Chapter 7: Managing distress in prostate cancer: a qualitative feasibility study into the design of a novel psychological support intervention for managing distress in prostate cancer.

I was unfortunately unable to recruit a suitably sized sample of AS patients into a standardised MBSR intervention. This was despite the fact that the majority of patients approached during the recruitment phase articulating a strong sense of distress, fear, uncertainty and anxiety about their diagnosis and management with AS. To address this issue I decided to implement the previously discussed contingency plan I created in case it was not possible to recruit into the mindfulness trial. Thus the aim of this investigation was to conduct a qualitative study utilising a semi-structured interview approach to ascertain the subjective problems, concerns and anxieties of men being managed with AS and to determine what kind of support they would like to help them better manage such concerns. It was hoped that through doing so it would be possible to generate a far more accurate assessment of the kinds of support AS patients wanted and would be willing to recruit into and adhere to in a way that they were not for MBSR. A substantial dearth of such research currently exists within the related PCa and AS research and it was hoped that the unique nature of my findings would help the design and development of an AS support intervention that would provide AS patients with the specific types of psycho-educational support they required in a structure and format that would be acceptable for them to recruit into.

Chapter 8: The way forward and conclusion

The aim of this final chapter was summarise and conclude the findings of the current PhD and highlight the direction that I believe the future research into the management of depression and anxiety in AS should take, based upon the findings from Chapter 7.

Chapter 2

A Narrative Literature Review of Depression and Anxiety in Prostate Cancer

2.1. Research Objectives

1. To critically appraise the literature pertaining to the prevalence and consequences of depression and anxiety in generic prostate cancer across the treatment spectrum, from initial diagnosis to post-treatment follow up.

2. To determine whether enough research currently exists to allow for the development of a rigorous systematic review and meta-analysis.

3. As this thesis will focus primarily on PCa patients being managed with AS, it was also my aim to provide an initial insight into the foundation of evidence into the prevalence of depression and anxiety specifically within PCa patients being managed with AS.

2.2. Introduction and Overview

Depression and anxiety are common psychological conditions to be experienced by cancer patients (Pasquini & Biondi, 2007). Historically, the relationship between cancer and psychological distress dates back to as early as the 4th century B.C. when Hippocrates first identified that patients suffering from cancer, then a newly discovered disease, were prone to experience lethargy, reclusiveness and despair (Gelder et al., 1998).

The complex relationship between cancer and psychological health has continued to intrigue physicians and psychologists ever since (Berrios, 1998; Alexander & Selesnick, 1996). From the mid-nineteenth century, systematic and controlled investigations into the causes and prevalence of depression and anxiety in cancer patients were being conducted (Berrios, 1998). The level of interest within this field of psycho-oncology has continued and has experienced a relative explosion of growth over the last three decades (Sellick & Crooks, 1999; Pasquini & Biondi, 2007).

The upshot of this research is that the foundation of knowledge relating to our understanding of the causes, prevalence and consequences of depression and anxiety within oncological care is large. The majority of this research has emphatically and unequivocally demonstrated strong positive correlations between those cancer patients presenting with depression and anxiety and a higher prevalence of both physical and psychological side effects.,(DiMattoe et al., 2000; McDaniel et al., 1995; Pirl et al., 2002). However, the direction of this association is not clear (Stark & House, 2000) and

it is possible that a higher prevalence of physical and psychological side effects may be responsible for a higher prevalence of anxiety and depression, rather than the other way around.

Unfortunately**,** the distribution of the research within this area is far from even. Certain cancer sites, most notably breast, colon and lung cancer, have generated the vast majority of data (Pirl et al., 2008; Reich et al., 2008; Weitzner, Meyers, & Byrne, 1996**;** Wellisch et al., 2002). The associated danger of this is that researchers, physicians and allied health care professionals working within the field of oncology may generalise and apply the findings from these cancer sites to other less well researched ones. Indeed, strong evidence exists to suggest that physicians carry their experiences and preconceptions of depression and anxiety in one group of cancer patients to another, irrespective of variations in the latter population's gender, age or cancer site (Davidson & Meltzer-Brody, 1999).

One particular cancer site that is heavily under researched in this area is prostate cancer (PCa). This shortfall of research is a significant one (Dale et al., 2005; Bennett & Badger, 2005). Whereas multiple literature reviews into the prevalence of depression and anxiety have been conducted within other cancer sites (Fann et al., 2008; Reich et al., 2008), very few exist relating specifically to PCa. This has resulted in a lack of synthesis of the previously conducted research, making it harder for the pertinent points from such research to be interpreted and the evidence employed within a clinical context. Consequently, what research does exists has had a minimal impact upon clinical practice, resulting in a lack of awareness about, and support for, the psychological requirements of PCa patients.

Thus the aim of the current literature review was to address this issue and provide an initial critical appraisal of the current foundation of research relating to the prevalence of depression and anxiety within PCa across the treatment spectrum. This would allow me to determine whether enough research evidence currently exists to allow for the running of a systematic review and meta-analysis into the prevalence rates of depression and anxiety with PCa, data that is currently missing in the foundation of related PCa research.

Additionally, because the aim of this PhD was to focus on the assessment and management of depression and anxiety specifically within AS patients, it was also the aim of this review to provide an initial overview of the foundation of research into depression and anxiety specifically within AS patients.

Whilst overviewing the literature, it became quickly apparent that the previously conducted research had been undertaken in three distinct categories:

1. Pre-Treatment: Depression and anxiety experienced by PCa patients prior to the initiation of treatment.
2. On-Treatment: Depression and anxiety experienced by PCa patients whilst undertaking treatment.
3. Post-Treatment: Depression and anxiety experienced by PCa patients after the completion of treatment.

To ensure that the current review was undertaken in a logical and coherent manner, each of these three categories were reviewed individually before providing a summary of the research both collectively and in context.

2.3. Depression and anxiety in PCa patients prior to treatment

Sociological research within the field of oncology has revealed that in the majority of non-medically trained individuals, cancer is synonymous with death (Seale, 1995). It is thus unsurprising that in the period of time between initial cancer diagnosis and subsequent treatment, newly diagnosed patients are prone to experience debilitating alterations to their psychological health and wellbeing as they process the ordeal ahead of them (Pasquini & Biondi, 2007; Sharpe et al., 2004).

Paradoxically this is a view both supported and discredited by the small amount of PCa research available. Such research suggests that between 0-26% and 8-31% of PCa patients develop clinically meaningful levels of depression and anxiety, respectively, prior to the initiation of treatment (Bisson et al., 2002; Gerbershagen et al., 2008; Soloway et al., 2004; Dale et al., 2009; Berry et al., 2006). However, the primary factors responsible for the large variation in these data are still much debated (Bisson et al., 2002; Gerbershagen et al., 2008; Berry et al., 2006).

In an often cited investigation, Bisson et al., (2002) observed that men with recently diagnosed localised PCa who had yet to undergo treatment experienced extremely low levels of depression and anxiety in comparison to both general cancer patients and normative values. In their sample of 88 participants, it was observed that only 8% were experiencing clinical anxiety whilst none were deemed to have depressive symptomology.

In their investigation, Bisson et al., (2002) utilised the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), an extremely well validated and reliable assessment tool (Love et al., 2002; Ibbotson et al., 1994). However, their decision to utilise a higher cut-off threshold score on the HADS for both the depression and anxiety subscales is partly responsible for prevalence data observed. The majority of cancer research utilising the HADS has selected a threshold score of eight to identify caseness, above which the patient can be deemed to be suffering from clinically meaningful depression and anxiety (Zigmond & Snaith,

1983). Bisson chose instead to utilise a caseness threshold of 10. In doing so they limited their study to identify only men suffering from much more severe depression and anxiety. Such an approach risks missing the identification of many men who may be experiencing lower but still meaningful levels of psychological distress (Moynihan, 2002; Zakowski et al., 2003). Indeed, if the lower HADS threshold of eight is applied to the Bisson et al., (2002) results, the prevalence of depression and anxiety rises to 5% and 22% respectively. Such data are much more in keeping with, if still slightly lower than, the majority of the previous research within this area (Burnet et al., 2007; Ene et al., 2006; Cliff & MacDonagh, 2000).

Previous commentaries have suggested that PCa patients may experience higher levels of disease related anxiety in comparison to other cancer patients (Dale et al., 2005). Such a rationale is founded upon the fact that the threat of 'de-masculinisation', a commonly perceived side effect of PCa treatment, is extremely anxiety inducing to men (Chapple & Ziebland, 2002). The small foundation of research that exists within this area has observed that PCa patients presenting with clinically meaningful anxiety are prone to select treatment options that increases their long term exposure to higher levels of treatment toxicity for no likely gain in survival and experience less overall satisfaction with those choices (Dale et al., 2009; van Tol-Geerdink et al., 2006).

For example, a novel investigation, Dale et al., (2009) assessed the relationship between PCa specific anxiety and the early initiation of hormone therapy in older patients experiencing biochemical recurrence (BRC) of PCa. In their investigation, the authors recorded the date that each patient presented with BRC and recorded baseline levels of PCa specific anxiety. Anxiety measures were then recorded at each subsequent clinic appointment until hormone therapy (androgen deprivation therapy; ADT) was initiated. The rationale for this study was that ADT is associated with high levels of toxicity, the side effects of which include weakened bone composition, muscular dystrophy, increased risk of cardiovascular morbidity, reduced liver functioning and significantly lowered quality of life (Lubeck et al., 2001; Berruti, Dogliotti & Terrone, 2001; Dacal, Seraika & Greenspan, 2006). Given the lack of conclusive evidence suggesting that the early initiation of ADT is associated with increased life expectancy, PCa patients who choose to begin ADT earlier than is clinically necessary risk exposing themselves to extremely high levels of toxicity for no apparent gain.

The crucial outcome of the Dale et al., (2009) study was that in multivariate logistical regression analyses, clinical levels of pre-treatment PCa specific anxiety, which was evident in 22% of participants, was the most robust predictor of early ADT initiation. More specifically, patients with clinically significant anxiety initiated ADT fourteen months earlier than non-anxious patients. These results indicate that older PCa patients who are clinically anxious are at a heightened risk of initiating ADT earlier than is clinically

necessary, exposing themselves to the associated toxicities of this treatment for over a year longer than their non-anxious counterparts.

Similar results were observed by van Tol-Geerdink et al., (2006) who revealed that men diagnosed with localised PCa who were clinically depressed and anxious placed significantly more emphasis on undergoing treatment with curative intent. When provided with a choice, the 21% and 14% of patients suffering from anxiety and depression were more likely to choose a higher dose of radiation therapy that offered an increased chance of cure, but was associated with increased physical side effects, than men who were not depressed or anxious.

Why depressed and anxious PCa patients appear to be more inclined to select radical potentially curative treatment is unclear. It has been suggested that one of the most predominant underlying causes of psychological distress in both general cancer patients and PCa patients is a fear of death (Dale et al., 2005; Seale, 1995). If so, then PCa patients with higher levels of depression and anxiety may be predisposed to select more intensive and radical treatment to help them gain some control over the primary cause of their distress (i.e. the risk of dying from PCa) by initiating a treatment plan that may have some positive impact upon increasing life expectancy. Such a view gains initial support from the fact that whilst prostate specific antigen (PSA) levels in the Dale et al., (2009) investigation were also significantly robust predictors of early ADT initiation, no significant correlation existed between rising PSA levels and increased anxiety. This suggests that the high levels of anxiety experienced by patients initiating ADT early was not associated with objective clinical facts, such as rising PSA levels, but more deep seated and unaccountable subjective issues.

Unfortunately, neither the Dale et al., (2009) nor the van Tol-Geerdink et al., (2006) investigations continued to assess depression and anxiety after the initiation of treatment. As a result it is currently not possible to ascertain whether psychological distress would have fallen after the radical treatment options had been initiated which, one speculates, would have afforded the patient a sense of regaining a degree of control over their disease.

Based on this evidence it would appear that in many cases, treatment selection is heavily influenced by the psychological health of the patient. If so, screening for depression and anxiety prior to treatment selection could go some way in ensuring that PCa patients make informed treatment decisions based on objective clinical facts, and not ones that are impacted upon, either consciously or subconsciously, by the presence of high levels of psychological morbidity.

2.4. Depression and anxiety in PCa patients whilst on-treatment

Significant reductions in the psychological well-being of generic cancer patients undergoing treatment are commonly observed and well reported (Ahles & Saykin, 2008; Sharifi, Gulley & Dahut, 2005). In the majority of cases, these reductions are a consequence of treatment induced side effects, prolonged periods of hospitalisation and a perceived lack of independence and worth (Pasquini & Biondi, 2007). However, the foundation of knowledge relating to the impact of treatment on the psychological health of PCa patients is limited.

Current treatment options for PCa include radical prostatectomy, radiotherapyand active surveillance (AS). All but the latter are classified as radical treatments whereas AS is utilised in patients with localised PCa who present with slow growing indolent tumours. With the popularisation and increased use of AS for the management of localised PCa in recent years, much debate exists regarding whether it should be classified as an active treatment modality as opposed to a passive, pre-treatment option (van den Berg et al., 2009). Whilst this debate continues, the current review will classify AS as an active treatment option based upon the fact that the patient has been clinically assessed and placed onto a suitable, albeit non-interventional, treatment pathway and as such will classify all studies utilising patients undergoing AS as being on-treatment. For the sake of clarity, the research relating to each treatment modality will be assessed independently.

2.4.1. The prevalence of depression and anxiety during active surveillance

To date only four investigations have attempted to measure depression and anxiety specifically in patients being managed with AS (Burnet et al., 2007; van den Berg et al., 2009; van den Berg et al., 2010; Steineck et al., 2002). In these investigations, the rationale driving the research was the view that patients undergoing AS are at an increased risk of developing psychological distress through having to live with what is essentially an untreated cancer (Pickles et al., 2007).

Whilst such a rationale appears plausible, Burnet et al., (2007) found this not to be the case. The authors observed that PCa patients' undergoing AS experienced no significant increase in the prevalence of depression and anxiety in comparison to patients undergoing radical treatment. As a result of these findings, the Burnet et al., (2007) investigation is commonly cited in the related research as evidence that AS does not predispose PCa patients to higher levels of psychological distress.

Despite the lack of statistically significant differences in the levels of depression and anxiety experienced by the different treatment groups in the Burnet et al., (2007) investigation, it is still important that the AS patients experienced over twice the level of anxiety as patients undergoing radical treatment. Only 10% of the patients undergoing radical intervention were classified as clinically anxious in comparison to 21% of the patients being managed with AS. Whilst such a difference may lack statistical significance, primarily due to the small sample size of this single centre study, it is still of key clinical importance as it suggests that patients opting for and undergoing AS experience twice the prevalence of anxiety as those treated radically. .

Such a view gains additional support from the fact that in the Burnet et al., (2007) investigation, recruitment was not randomised and each participant had already selected their treatment option prior to recruitment. It is possible that men inherently predisposed to experience higher levels of anxiety would more naturally have selected immediate radical intervention, such as surgery or radiotherapy, that are potentially curative. Conversely, it can be speculated that the participants opting for AS were less likely to be anxious given the nature of the treatment they selected. Whilst no research exists to support this view, if less anxious men were more likely to select AS but subsequently developed higher levels of anxiety, as in the Burnet et al., (2007) investigation, then the anxiety inducing nature of AS may be heavily underestimated. Unfortunately the absence of supporting research means that it is currently not possible to ascertain whether or not this was the case. Additional longitudinal research that assesses anxiety levels prior to treatment selection would be hugely beneficial to determine if lower anxiety increases a patient's predisposition to select AS over radical treatment

More recently, van den Berg et al., (2009 & 2010) has added to the research base regarding the levels of psychological distress experienced by PCa patients during AS. Whilst no comparison groups were recruited with which to compare the AS patients, the authors observed that 8% of patients undergoing AS were classified as clinically depressed and 17% were deemed to be suffering from clinically meaningful levels of PCa specific anxiety. These figures are similar to those reported by Burnet et al., (2007) in that AS patients presented with lower levels of depression and high levels of anxiety.

Interestingly, a key component of the van den Berg et al., (2009 & 2010) investigations was to assess the impact of conflicts arising from treatment selection on the levels of depression and anxiety experienced. Utilising the Decisional Conflict Scale (DCS, O'Conner, 1995), a well validated and reliable instrument (Koedoot et al., 2001), it was observed that men with lower DCS scores reported having significantly lower levels of depression and anxiety. In other words, men who selected AS based upon their own views and beliefs, and not on those of their treating physician, were more likely to report satisfaction with their

treatment selection, resulting in a lower prevalence of psychological distress. Conversely, men who believed that their physician was the most important factor in their decision to select AS had significantly higher DCS scores, suggesting that such men has much more doubt regarding the merits of AS as their initial treatment option.

With oncologist and urologists increasingly leaning towards the use of AS as the primary management approach for men with localised PCa (Bastina et al., 2009), the findings observed by van den Berg et al., (2009, 2010) are important. If men who have less doubt regarding the use of AS report a lower prevalence of depression and anxiety, then ensuring that men feel central to the treatment selection process may represent a crucial method of reducing depression and anxiety in PCa patients during the distressing task of selecting treatment.

However, the above has highlighted that the foundation of research evidence into the psychological wellbeing of patients being managed with AS is extremely limited and further investigation is clearly warranted. This is particularly true given the increasing number of men being diagnosed with low grade, localised PCa who do not require radical intervention and can be managed effectively and safely with AS.

2.4.2. The prevalence of depression and anxiety during androgen deprivation therapy (ADT).

Androgen deprivation therapy (ADT), a treatment modality traditionally reserved for those with metastatic disease, is now routinely administered to PCa patients with less advanced cancer staging (Sharifi et al., 2005). Indeed, it is quickly becoming one of the most common treatment modalities for men with locally advanced PCa (Sharifi et al., 2005). Unfortunately, little research exists regarding the consequences of ADT initiation on the psychological health of PCa patients.

Stone et al., (2000) undertook one of the first investigations into the prevalence of depression and anxiety in PCa patients undergoing ADT and observed that at the initiation of treatment, 15% and 3% of patients were suffering from clinical anxiety and depression, respectively. Interestingly however, there were no significant increases in either depression or anxiety over the duration of ADT treatment (three months) despite there being a significant increase in cancer related fatigue. In light of such findings, Stone et al., (2000) concluded that whilst additional research is clearly required, a three month ADT treatment plan had no negative impact upon psychological health.

However, these findings should be interpreted with caution. When the participants completed the second series of questionnaires (after completing three months of treatment), they had already received clinical

confirmation of a positive response to ADT treatment. Median PSA levels had fallen from 19.8ng/ml at the start of the investigation to 1.0ng/ml at the time of follow up. It is possible that the participants felt considerably less psychological distress at follow up due to the knowledge that they were responding positively to their therapy. Indeed, research exists to suggest that patient reported perceptions of psychological distress are greatly diminished upon confirmation of positive treatment responses (Bocchieri, Meana & Fisher, 2002). This would suggest that ADT related side effects, which have been shown to induce psychological distress (Herr & O'sullivan, 2000), may cease to be so significant to overall psychological health if the patient knows their tumour is responding to treatment.

Such findings are in contrast to those observed by Pirl et al., (2002) who demonstrated that patients undergoing ADT experienced a high prevalence of depression, ranging from 13.3% as assessed by the Beck Depression Inventory and 12.8% via the Structured Clinical Interview for DSM-IV (SCID). However, a crucial finding observed was that depression was not significantly correlated to important clinical markers of disease progression such as rising PSA levels. For example, mean depression in men with stable, treatment responsive PCa was 13.9% compared to 14.3% in men with progressive PCa that was androgen independent. This suggests that in men receiving ADT, knowledge of disease progression is not significantly distressing to them.

Perhaps unsurprisingly, Pirl et al., (2002) also observed that current depression was significantly predicted by previous depression. Patients with a past history of depression had a prevalence rate of 83.3% for current major depression whilst undergoing ADT, and every patient receiving a SCID diagnosis of major depression also had a past history of depression. Such findings suggest that in men receiving ADT, a past history of depression represents a significant risk factor for current depression and as such must be assessed and utilised as a crucial method of identifying patients who may be at risk of developing psychological distress whilst undergoing ADT.

Whilst a past history of depression has been shown to be a key risk factor for current depression in many cancer populations (Nordin et al., 2001; Lanksy, List & Herrman, 1995), in almost all cases depression has positively correlated to clinical disease markers such as cancer growth and progression. It is thus fascinating that in the Pirl et al., (2002) investigation the development of depression whilst undergoing ADT was not associated with crucial clinical markers of disease progression. It would seem plausible that if current depression was not associated with specific disease characteristics then it was likely to have been a result of the patients' response to ADT and its related side effects. This seems particularly likely given that mean time on ADT was over three years. Strong evidence exists to suggest that the high level of depression experienced by hypogonadal men without cancer is due to the reduction in circulating

testosterone levels (Barrett-Connor et al., 1999). For the participants in the Pirl et al., (2002) investigation, the high levels of depression observed may be due, at least in part, to the significant reduction in circulating testosterone levels they were exposed to for over three years.

Interestingly, in a similarly designed follow up study, Pirl et al., (2008) provided additional support for the view that depression in men receiving ADT is likely to be influenced by endocrinological factors. Specifically, the authors investigated whether men undergoing a 12-month hormone therapy treatment programme for PCa experienced different levels of depression dependent upon the type of hormone therapy they received. Group one received leuprolide, the most commonly prescribed form of ADT and the type utilised in their earlier investigation (Pirl et al., 2002). The second group received bicalutamide, a non-steroidal anti-androgen compound. Because the latter does not decrease circulating testosterone levels, the authors hypothesised that patients undergoing bicalutamide treatment would experience a significantly lower prevalence of depression over the 12-months treatment period.

Cross-sectionally, the mean prevalence of depression across both groups was high, ranging from 10.4% at baseline, increasing to 16.7% at 6-months and falling back to 10.4% at 12-months. However, the key finding was that the group utilising leuprolide experienced significantly higher levels of depression than the bicalutamide group at both six and twelve months, despite their being no significant differences between the groups at baseline. It is possible that a key factor responsible for the higher levels of depression experienced by the leuprolide group was the reduction in circulating testosterone. Whilst clinical debate exists regarding the collective efficacy of leuprolide versus bicalutamide for the treatment of PCa (Tyrrell et al., 1998; Boccardo et al., 1999), these findings suggest that when deciding upon which type of hormone therapy to undergo, it may be beneficial to take into account the psychological health of the patients and in particular, whether they have a past history of depression.

However, it is likely that the relationship between hormone therapy treatment type and depression prevalence is influenced by a variety of factors other than endocrinological ones. Specifically, the leuprolide group also experienced a significant increase in cancer related fatigue (CRF) at both baseline and 12-month follow up in comparison to the bicalutamide group. It is just as feasible that the higher prevalence of depression in the former group was due to the high levels of fatigue they were experiencing. Much debate exists regarding whether CRF induces depression or whether a depressed state induces CRF (Jacobson, Donovan, & Weitzer, 2003). In light of the paucity of research addressing this issue within PCa, it is currently impossible to ascertain whether or not this is the case. Further research is clearly warranted.

2.4.3. The prevalence of depression and anxiety across multiple treatment modalities

Few investigations have assessed the prevalence of depression and anxiety in populations of PCa patients undergoing varying treatment options. Interestingly, one of the few investigations that has attempted to do so recorded the highest prevalence of depression in any of the published research to date. In that study, Dirksen et al., (2009) assessed the relationship between depression and insomnia in a sample of PCa patients with varying stages of disease progression undergoing a variety of treatment options that included prostatectomy, radiotherapy, hormone therapy and chemotherapy. It was observed that 51% of the participants were classified as clinically depressed using the Centre for Epidemiological Studies-Depression Scale (CES-D).

Several possible explanations exist for this exceptionally high prevalence rate. Most notably, 51% of the participants recruited into the investigation were suffering from Stage IV metastatic disease. Given that such men are living with an incurable cancer with a limited life expectancy (Berthelet, Pickles & Lee, 2005), it is unsurprising that the prevalence of depression was so high. Indeed, additional research lends support to the fact that cancer patients with advanced disease display significantly higher levels of depression than those with localised, early stage cancer (Spiegel & Giese-Davis, 2003).

The clinical implications of such findings are large as it suggests that the prevalence of depression and anxiety in PCa, commonly cited as between 15%-25%, may represent a gross under-estimation based upon the fact that such research has been obtained predominantly, if not exclusively, from men with localised disease. The findings observed by Dirksen et al., (2009) suggest that in men with metastatic disease the prevalence of depression may be twice as high. These findings suggest that men presenting with metastatic disease are highly susceptible to psychological morbidity and warrant early screening for depression once their disease has progressed to an advanced stage.

2.5. Depression and anxiety in PCa patients after the completion of treatment.

The physical side effects associated with radical treatment for PCa are well documented (Lev, Eleer & Gejerman, 2009) and include urinary incontinence, impotence and bowel dysfunction, depending on which treatment modality is undertaken. These side effects typically manifest relatively soon after the initiation of treatment. Patients who undergo radical prostatectomy are likely to experience sexual and urinary dysfunction immediately after the completion of surgery whilst patients undergoing radiation therapy or hormone therapy begin to see increases in bowel dysfunction within the first two to three weeks of treatment (Kirby & Taylor, 2008).

A crucial issue surrounding PCa treatment is that the side effects can persist for an extremely long time after the completion of treatment and can, in some instances, be permanent (Kirby & Taylor, 2008). Whilst research into generic cancer care has suggested that patients are prepared to accept treatment induced side effects whilst actually undergoing treatment, they are little prepared for the continuation of them once treatment ceases (Carelle et al., 2002). For PCa patients who have completed treatment, the continued presence of disturbing physical side effects for many months and years is likely to be distressing to them. It is therefore unsurprising that PCa patients are vulnerable to the development of depression and anxiety in the months and years after the cessation of treatment.

Several investigations have been undertaken with the aim of assessing the prevalence of depression and anxiety in post-treatment PCa patients who have undertaken different treatment modalities (Namiki et al., 2007; Hervouet et al., 2005; Lim et al., 1995). Interestingly, the research had generally observed that the prevalence of depression and anxiety varies very little irrespective of the treatments undertaken. For example, Namiki et al., (2007) compared the prevalence of depression and anxiety in a sample of PCa patients who had undergone either radical prostatectomy (RP) or radiotherapy (RAD) two years previously. It was identified that both groups displayed very low prevalences of depression and anxiety on the Hospital Anxiety and Depression Scale (4.6 and 3.9 respectively). It was also reported that no significant differences were observed in the prevalence of depression and anxiety between the two treatment groups, suggesting that treatment type has very little influence on levels of long term psychological distress.

An important finding of the Namiki et al., (2007) investigation was that the participants who were experiencing clinical depression or anxiety presented with significantly worse urinary and bowel dysfunction. Given that all the participants had completed treatment over 30 months previously, it is unsurprising that continued urinary and bowel dysfunction so long after the cessation of treatment was associated with increased levels of psychological distress. However, these findings are unusual as research suggests that such symptoms usually dissipate within the first 12-months post treatment. Thus why specific patients in the Namiki et al., (2007) investigation continued to experience such problems for so long is unclear. One possible explanation could be the relatively high age range of the recruited participants. Whilst the mean age of the RP and RAD groups were 69 and 76 respectively, the patient age range rose to as high as 86. Given that over 15% of elderly men without cancer aged over 80 experience urinary and bowel dysfunction (Srulevich & Chopra, 2007), such symptoms, and the psychological distress associated with them, could be due to age related decline and not just PCa treatment induced side effects.

In an investigation again utilising radical prostatectomy (RP) and radiotherapy (RAD) patients, Lim et al., (1995) observed very similar findings to those reported by Namiki et al., (2007), lending support to the view that long term treatment induced side effects are associated with a higher prevalence of depression. Whilst Lim et al., (1995) reported no significant differences in the prevalence of depression between the RP and RAD patients, higher levels of urinary, bowel and sexual dysfunction were significantly associated with a higher depression score. Additionally, the majority of the participants had completed treatment between 12-18 months previously. Such results, like those observed by Namiki et al., (2007), suggest than not only do treatment induced side effects persist for much longer than is traditionally believed, but that such side effects are significantly associated with an increased prevalence of depression.

An interesting finding reported by Lim et al., (1995) was that 96% of the RP group were impotent at the time of entry into the investigation and reported significantly worse sexual functioning in comparison the RAD group. Such findings are among the highest rates of surgery induced impotence recorded in PCa patients to date. Whilst these high impotence rates can be predominantly explaining by the lack of nerve sparring techniques utilised, it is intriguing that the RP patients reported no significant increase in depression compared to the RAD group, of whom only 54% were impotent. Given the widely reported view that post-treatment depression in PCa patients is often due to a reduction in sexual potency (Soloway et al., 2004), these findings offer a new perspective on PCa patients views of the value of sexual relationships and suggest that a perceived lack of sexual potency is not necessarily associated with an increase in depressive symptomology.

Such a view is further supported by the finding that 98% of the RP group and 87% of the RAD group were fully satisfied with their treatment decision and subsequent outcomes and would select and undergo the same treatment again. In light of the significant reduction in physical functioning recorded by both groups, these data suggest that PCa patients may be prepared to sacrifice quality of life and sexual function in favour of selecting a treatment option that may provide them with the best chance of a cure, even if such treatment is associated with prolonged (12-18 months) periods of physical impairments.

In contrast to the above, Hervouet et al., (2005) suggests that post-treatment depression and anxiety is a factor of, and is significantly influenced by, the specific treatment options undertaken. Investigating patients who had undergone radiotherapy (RAD), radical prostatectomy (RP) or brachytherapy (BR) over 22 months previously, it was observed that the participants who underwent radiation treatment experienced significantly higher levels of depression (20.9%) in comparison to the RP (12.1%) and the BR (16%) groups.

Tellingly, the radiotherapy group also reported significantly higher levels of cancer related fatigue in comparison to the other two groups. Fatigue is a well-documented side effect of radiation therapy and many investigations have highlighted that patients undergoing radiotherapy develop clinical depression (Howlett et al., 2010; Greenberg et al., 1993). It seems possible that for PCa patients treated with radiotherapy, depression and fatigue may be related.

Another key finding observed by Hervouet et al., (2005) was that of the three treatment groups, the patients who underwent radical prostatectomy had the lowest reported prevalence of depression despite experiencing the highest levels of sexual dysfunction. This again suggests that post-surgery sexual dysfunction is not necessarily associated with an increase in depressive symptomology. Such findings offer clear comparisons with those observed by Lim et al., (1995) who also reported that despite experiencing significantly greater sexual dysfunction, prostatectomy patients experienced no significant increase in psychological distress compared to patients who maintained post-treatment sexual potency. In combination, such research suggests that the traditional view of PCa patients wishing to maintain post treatment sexual functioning at all costs (van Tol-Geerdink et al., 2006), even at the expense of an increased life expectancy (Singer, Tasch & Stocking, 1991), may be based more heavily on anecdotal sociological stereotypes than on objective clinical facts.

2.6. Summary and Conclusion

This narrative literature review has revealed that to date a clinically important level of research into the assessment of the prevalence of depression and anxiety within the realm of PCa exists. The data is such that if it could be effectively summarised it would be likely to impact substantially on the clinical management of PCa. The evidence is certainly sufficient to warrant a rigorous systematic review and meta-analysis into prevalence rates. Doing so would allow for the provision of a more definitive estimate of depression and anxiety prevalence in PCa, at various treatment stages, which would allow those working within the field of PCa to become more aware of the likelihood of depression and anxiety in the spectrum of PCa patients they treat. Recent meta-analyses of depression and anxiety currently exist for many other cancer sites and the absence of such date specifically for PCa is an important omission. Across the continuum of research appraised within this review, the prevalence of depression and anxiety has been shown to fluctuate relatively widely. Whilst some investigations reported no prevalence of depressive symptomology at all in PCa patients (Bisson et al., 2002), others observed that over 50% were deemed to be suffering from clinical depression (Dirksen et al., 2009). Similarly, anxiety prevalence was reported to be as low as 8% (Bisson et al., 2002) and as high as 31% (Gerbershagen et al., 2008).

The reasons for this wide disparity are many. In several cases it can be explained by the methodological designs utilised within the investigation. Specifically, whilst the use of reliable and well validated questionnaires such as the Hospital Anxiety and Depression Scale is to be applauded, investigator based decisions on which cut-off threshold to utilise can alter the prevalence of depression and anxiety by over 5% and 16%, respectively (Bisson et al., 2002). To ensure the applicability and generalisability of future research, it would be beneficial if accepted cut-off scores on often used questionnaires could be standardised.

Similarly, it is crucial that clear distinctions are made between data that are statistically significant and those that are clinically relevant and meaningful. For example, research has concluded that AS has no significant impact on anxiety in comparison to hormone therapy or radiotherapy (Burnet et al., 2007). However, this was in spite of the fact that AS patients presented with over twice the prevalence of clinical anxiety in comparison to their counterparts undergoing radical treatment. Whilst Burnets' investigation may have lacked sufficient participant numbers to identify the statistical significance of these findings, they are still clinically important in pointing to the potential predisposition of AS patients to develop higher levels of anxiety in comparison to patients undergoing radical intervention.

It was also an aim of this chapter to provide an initial insight into the foundation of evidence into the prevalence of depression and anxiety specifically within AS patients. To date, it appears that only 4 investigations have measured depression and anxiety in AS patients (Burnet et al., 2007; van den Berg et al., 2009; van den Berg et al., 2010; Steineck et al., 2002). With the increasing use of PSA screening in the UK and an aging population, the majority of PCa diagnoses made in the UK involve cancer that is localised and indolent (Cancer Research UK, 2010). For men diagnosed with such a condition, AS is the recommended treatment option (NICE, 2014). This review has highlighted that very little research has attempted to assess the prevalence of depression and anxiety specifically within this patient cohort. However, the limited research that is available suggests that men placed onto surveillance experience over twice the prevalence of clinical anxiety as men being treated radically (Burnet et al., 2007). In light of the increasing utilisation of AS within the UK it would appear imperative that a more robust and definitive assessment of depression and anxiety in this cohort of PCa patients be undertaken.

Similarly, all of the research included within this review has been undertaken predominantly on white, middle class men. Black men typically make up less than 8% of all of the recruited participants in the generic PCa research whilst Asian men account for less than 2% (Ullrich et al., 2003; Dirksen et al., 2009). This represents a substantial gap in our understanding of the psychological impacts of PCa as no

research exists to suggest whether ethnic minorities are at an increased or decreased risk of developing psychological distress in comparison to Caucasians. This is an important issue as Afro-Caribbean men have been shown to be at substantially higher risk of developing PCa compared to Caucasians (Ben-Shlomo et al., 2008). Thus to ensure that research findings derived almost exclusively from white patients are not generalised to ethnically diverse patients groups, it would appear vital that focused research on the latter populations be undertaken to address this issue.

The steady increase in research addressing the prevalence of depression and anxiety in PCa patients in recent years is reassuring and suggests that the desire to better understand the psychological requirements of this group of older, chronically ill men is beginning to grow. The current literature review has identified that a sufficient foundation of evidence exists to warrant the running of such a systematic review and meta-analysis. It was hoped that through doing so it would be possible to generate a more definitive estimate of depression and anxiety prevalence across the spectrum of PCa patients.

Chapter 3

Depression and Anxiety in Prostate Cancer: A Systematic Review and Meta-Analysis of Prevalence Rates

3.1. Research Question and Objectives

Research Question: What is the prevalence of clinically meaningful depression and anxiety among prostate cancer patients and how does this prevalence vary across the treatment spectrum?

Research Objectives:

1. The research base evaluating the prevalence of depression and anxiety within PCa is growing steadily and a sizeable body of clinically relevant research currently exists. Unfortunately these data have yet to be subjected to rigorous systematic review and meta-analysis. The primary objective of the current investigation was to address this issue and conduct the first systematic review and meta-analysis of depression and anxiety prevalence rates in PCa.

2. It is as yet unclear what stages of the PCa journey patients find most distressing. Were this known, or at least better understood, it would allow health care professionals to be more proactive and aware of what stages of treatment patients are most likely to experience depression and anxiety. This would allow the health care team to "risk-adapt" their psychological screening and support processes. The second objective of the current meta-analysis was to address this issue and provide an initial baseline estimate of how the prevalence of depression and anxiety varies across the three key stages of the treatment trajectory in PCa; pre-treatment, on-treatment and post-treatment.

3. The overriding aim of the current PhD was the assessment and management of depression and anxiety specifically within AS. However, it was firstly important to understand how prevalent psychological distress was across the full spectrum of PCa treatments. The third aim of this study was to allow me to better place into context and determine how the prevalence rates of depression and anxiety obtained specifically for AS through the cross-sectional survey conducted in Chapter 4 compared with those observed for other management strategies used in PCa. To help maximise

the relevance of this research aim to AS, it was also my aim to extract all depression and anxiety data specifically for PCa patients with localised disease. Performing a sub-group analysis for localised PCa in this way would allow me to compare how the depression and anxiety prevalence data collected in Chapter 4 compares to that observed in the generic population of PCa patients with localised disease.

4. In the literature review conducted in the previous chapter I identified a substantial shortfall of research into the psychological wellbeing of PCa patients being managed with AS. A fourth aim of the this systematic review was to extract all data relevant to AS patients that may have been reported within studies that evaluated PCa as a whole and thus may not have been identified in my narrative review chapter. Likewise, it was also my aim to perform a sub-group analysis for depression and anxiety prevalence specifically in those studies that only recruited AS patients. This would further assist the interpretation of the results generated in Chapter 4.

3.2. Introduction

3.2.1. Introduction to depression and anxiety in cancer

Cancer patients have been shown to commonly experience substantial emotional and psychological upheaval at many points during the course of their disease, from pre-treatment through to treatment and subsequent follow up (Pasquini & Biondi, 2007). Patients face the prospect of invasive and potentially painful treatment, changes to their role within the family, work and society at large, financial pressures, alterations to body image and the possibility of death. Unsurprisingly, all of these factors have been identified as key components relating to the development of depression and anxiety within this patient population (Bailey et al., 2005; Sharpe et al., 2004).

The prevalence of depression and anxiety within generic cancer patients has been extensively researched over the previous three decades. The collective consensus from this research is that between 20-50% of patients will develop clinically significant levels of depression, whilst up to 90% can expect to experience clinically meaningful levels of anxiety over the course of their disease (Pasquini & Biondi, 2005; Noyes, Hold & Massie, 1998). However, these prevalence rates have been shown to vary greatly depending upon cancer site and stage, patient gender, age, co-morbidity, treatments undertaken and overall prognosis (Lorant et al., 2007; Jones et al., 2003; Hann et al., 2001).

Whilst prevalence rates may vary widely, the impact of depression and anxiety on subsequent physical and psychological functioning is far less equivocal (Avrahan & Ben-Eliyahu, 2007). It has been observed that clinically depressed and anxious cancer patients have lower treatment compliance, poorer treatment outcomes, lower quality of life, experience increased periods of hospitalisation and have poorer 5-year survival rates than their non-depressed and anxious counterparts (DiMattoe, Lepper & Croghan, 2000; McDaniel et al, 1995; Pirl et al., 2002; Watson et al, 1999).

A distinct paucity of research assessing the prevalence of depression and anxiety within certain cancer sites currently exists (Balderson & Towell, 2003). One such cancer that has generated little research interest within this area is prostate cancer (PCa). Indeed, several years ago, Bennet and Badger (2005) observed that the assessment of the prevalence of depression and anxiety in men with prostate cancer "has yet to be addressed adequately in the research literature" (p.545). Whilst this issue is slowly being resolved, it still represents a considerable void in our understanding of the management of this disease.

3.2.3. Depression, anxiety and prostate cancer

Whilst research specifically assessing depression and anxiety in PCa may be sparse in relation to that observed in some other cancer sites, a sufficient foundation exists to have a significant degree of clinical relevance. Unfortunately, the findings from this research have been plagued with high levels of heterogeneity which has limited the impact of the research upon clinical practice. For this situation to be remedied, a clearer synthesis of the data is required.

Given the longevity associated with the trajectory of PCa (over 70% of men can expect to be alive after 10 years; Office for National Statistics, 2007), it is likely that the onset of psychological distress within this population of men is not an acute threat that quickly passes but a chronic one with peaks and troughs of severity that occur at key stages of the cancer journey. Relating specifically to PCa, it is as yet unclear what stages of the cancer journey, from pre-treatment to post-treatment follow up, is most likely to induce depression and anxiety. Were this known, or at least better understood, a more personal, individualised and proactive approach to PCa patient support could be initiated based on each patients current stage of treatment.

Research from additional cancer sites has suggested that some of the most psychologically distressing periods for cancer patients occur during: 1. The time lapse between diagnosis and treatment (Leeuw et al., 2000). 2. Treatment implementation (Frick, Tyoroller & Panzer, 2007)

and 3. In the post-treatment follow up period as the patient faces the threat of recurrence (Deshields et al., 2006). If this information was available for PCa specifically, it would allow health care professionals to risk-adapt psychological screening, with more intensive screening and support being offered to the patient cohorts that are at a heightened risk of developing depression and anxiety based upon their current location on the treatment trajectory.

Thus there exists a clear need for a systematic overview of the related research focusing specifically on the varying prevalence rates of depression and anxiety in PCa at specific points of the cancer journey, from pre-treatment to post-treatment follow up. Such research would assist physicians and allied health care professionals in recognising not only the likely prevalence of depression and anxiety in their patients, but also at which points in time, over the course of the disease, they may be most at risk of developing these conditions.

Furthermore, one of the key aims of the programme of work making up this PhD was to more definitively define the prevalence of depression and anxiety specifically in PCa patients being managed with AS. Producing a meta-analytical estimate of depression and anxiety prevalence in generic PCa across the treatment spectrum would provide me with a means of comparing and contrasting the prevalence of depression and anxiety observed specifically in a cohort of AS patients (as generated in chapter 4) with those for generic PCa. This would in turn allow me to determine whether the prevalence rates produced specifically for AS patients were lower or higher than that estimated via the current meta-analysis.

The aim of the current systematic review and meta-analysis was to address these issues and provide the first initial estimate of the prevalence of depression and anxiety specifically within PCa as a function of treatment stage. Such information is currently lacking in the available published research.

3.3. Method

3.3.1. Eligibility criteria

Drawing upon the systematic review guidelines devised by the Centre for Research and Dissemination (2008), the eligibility criteria for studies entering into the current meta-analysis are listed below.

Study Design:

- Primary research studies that investigated and recorded the specific prevalence of depression and/or anxiety in PCa patients in full journal articles were eligible for inclusion.
- Studies published in conference proceedings, qualitative research, commentaries and discussions, letters, books, book chapters or research not published in the English language were excluded.

Population:

- The current meta-analysis was restricted to research focusing on individuals with a biopsy confirmed diagnosis of PCa. Studies failing to report the method by which the PCa diagnosis was made were rejected.
- If PCa patients were included within an investigation that recruited mixed cancer populations, the study was required to have reported data about the PCa patients as a distinct sub-sample.
- Where research included both the PCa patients and their spouses/partners in the investigation, the study had to report data about the PCa patients as a distinct sub-sample.

Outcomes:

- The primary outcome measure of the current meta-analysis was the percentage prevalence of depression and/or anxiety.
- Inclusion into the meta-analysis was restricted to those studies that reported data regarding the specific prevalence of depression and anxiety that had been measured and recorded using one (or more) of the accepted questionnaires (see section 3.2.2).
- Studies that reported depression and anxiety as a combined score (i.e. Hospital Anxiety and Depression Scale – Total Score) without also reporting their individual scores (i.e. Hospital Anxiety and Depression Scale – Depression and Anxiety subscales) were rejected from entry into the meta-analysis.

Treatments:

- Each study was required to provide clear definitions of the PCa treatments undertaken by the study participants.

- Each study was also required to specify when the PCa treatment took place (i.e. Pre-treatment: treatment that was due to be undertaken; On-treatment: treatment that was being undertaken during the time of the investigation or Post-treatment: treatment that had previously been undertaken).
- For Post-treatment investigations, it was a requirement that the authors specified the time lapse since treatment cessation.

Questionnaire Analysis:

Entry into the meta-analysis required that only data collected from questionnaires that provided specific, valid and reliable measurements of depression and/or anxiety were utilised (Section 3.2.2).

3.3.2. Questionnaire Analysis

Analysis of the questionnaires utilised in the previously conducted research into the psychological health of PCa patients revealed than over forty different types of questionnaire have been utilised (see Appendix 1). A large majority of these questionnaires (e.g. the SF-36, the Impact of Events Scale, the Mental Adjustment to Cancer Scale) were designed with the specific intention of measuring generic quality of life indices that encompass a wide variety of physiological and psychological conditions. However, such questionnaires do not provide specific measurements of depression and anxiety as distinct psychological conditions but rather include them as components of generic 'mental health', along with a variety of additional conditions such as nervousness, fear, restlessness and agitation. Consequently, a large majority of the research into psychological distress in PCa has reported generic 'mental health' scores as opposed to data relating specifically to depression and anxiety as unique psychological constructs.

As the current meta-analysis was undertaken with the specific intention of assessing depression and anxiety, it was crucial to ensure that only data collected from questionnaires that specifically measured depression and anxiety were identified, extracted and analysed. To that end, a series of questionnaire specific inclusion criteria, against which all of the identified questionnaires could be assessed, was created. This ensured that only studies utilising valid and reliable questionnaires that specifically measured depression and anxiety were entered into the data extraction

Questionnaire Eligibility Criteria

For data to be eligible for inclusion into the current meta-analysis, the questionnaires utilised to assess depression and anxiety in PCa patients must have fulfilled each of the following criteria:

- The questionnaire must have allowed for the specific and independent measurement of the prevalence of depression and/or anxiety.
- Established threshold information must exist for the depression and anxiety scores, above which a participant can be deemed to be clinically depressed or anxious.
- The concurrent validity of each questionnaire must have been assessed and deemed acceptable.
- The reliability of the questionnaire must have been assessed and deemed acceptable following test-retest assessment.

Accepted Questionnaires

The questionnaire eligibility criteria listed above was then applied to each of the 40 questionnaires initially identified. Of the original 40 questionnaires identified, 12 met all of the inclusion criteria and were thus deemed acceptable to provide valid and reliable depression and anxiety prevalence data for entry into the meta-analysis. A list of the accepted questionnaires follows:

1. Hospital Anxiety and Depression Scale (HADS)
2. Beck Depression Inventory (BDI)
3. Centre for Epidemiological Studies Depression scale (CES-D)
4. Memorial Anxiety Scale for Prostate Cancer (MAX-PC)
5. Stait -Trait Anxiety Scale (STAI)
6. Self Rating Anxiety Scale (SAS)
7. Self Rating Depression Scale (SDS)
8. Composite International Diagnostic Interview (CIDI)
9. Symptom Checklist-90 (SCL-90)
10. Effects of Prostate Cancer on Lifestyle Questionnaire (EPCLQ)
11. Brief Symptom Inventory (BSI)
12. Structured Clinical Interview for Depression (SCID)

3.3.3. Identifying Research Evidence

To maximise the diversity and scope of the literature search in the current review and to minimise the degree of publication bias encountered, multiple search strategies were utilised,

all of which are overviewed below. All searches were undertaken between September 2010 and December 2010.

- **Search Strategy Validity**

Database selection: Before beginning the research identification process, it was necessary to determine which electronic databases would be searched. To determine this I conducted a scoping exercise. Initially this involved looking through all the relevant Cochrane reviews and listing the databases they searched to identify their research evidence. The Cochrane reviews were utilised as the starting point in this exercise as they represent the gold standard of systematic review methodology and rigour. Once this process had been undertaken and a list of potential databases was created, I searched through other relevant peer reviewed non-Cochrane systematic reviews and meta-analyses to assess which databases they had utilised. In an iterative manner I progressed through this process until an initial comprehensive a list of electronic databases was created.

Once this list had been created I scheduled an appointment with a professional librarian at the Medical Sciences Library at Southampton General Hospital who was trained and experienced in search strategies and protocols. During my appointment with the librarian we discussed and modified my database selections based upon the librarians professional recommendations and in this way created a comprehensive and complete list of databases to search.

Electronic Database Searches

I searched six electronic databases for articles that met the above specified inclusion criteria using pre-specified search terms as listed in Table 1 below:

Table 1. Databases, Date Ranges and Search Terms Used to Identify Relevant Articles

Database	Date Range Searched	Search Terms
Ovid Medline	1950-2010	MeSH terms: Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)"
EMBASE	1980-2010	Free Text Key Words: "Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)" or "Psychological stress (EXP)" or "stress (EXP)" or "distress (EXP)" or "fear (EXP)" or "concern (EXP)" or "worry (EXP)".
AMED (Allied and Complementary Medicine)	1985-2010	Free Text Key Words: "Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)" or "Psychological stress (EXP)" or "stress (EXP)" or "distress (EXP)" or "fear (EXP)" or "concern (EXP)" or "worry (EXP)".
PsycINFO	1985-2010	Free Text Key Words: "Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)" or "Psychological stress (EXP)" or "stress (EXP)" or "distress (EXP)" or "fear (EXP)" or "concern (EXP)" or "worry (EXP)".
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982-2010	Free Text Key Words: "Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)" or "Psychological stress (EXP)" or "stress (EXP)" or "distress (EXP)" or "fear (EXP)" or "concern (EXP)" or "worry (EXP)".
Web of Science	1970 – 2009	Free Text Key Words: "Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)" or "Psychological stress (EXP)" or "stress (EXP)" or "distress (EXP)" or "fear (EXP)" or "concern (EXP)" or "worry (EXP)".

Reference List Searches

- To supplement the electronic database searches, I also conducted searches of the reference lists of previous reviews, key papers and relevant articles identified by the electronic search.

Hand Searches

Due to the time delay between the publication of articles in peer reviewed journals and their subsequent entry into electronic databases, a crucial element of the literature search process was to hand search recent copies of key journals to identify very recent articles that may not yet have been included or indexed by electronic databases. To allow for the systematic search of such journals, a full list of the most commonly cited journals identified by the electronic database search was created (see Table 2). The hard copies of these journals were then retrieved and the contents list visually scanned for any articles relevant to the current meta-analysis.

Table 2. List of Key Journals Hand Searched

Name of Journal	Issues Searched
Psycho-Oncology	September 2010, Volume 19, Issue 9 to December 2010, Volume 20, Issue 2.
British Journal of Health Psychology	September 2010, Volume 15, Issue 3 to December 2010, Volume 16, Issue 1.
British Journal of Urology International	September 2010, Volume 106, Issue 6b to December 2010, Volume 107, Issue 4.
Journal of Clinical Oncology	September 2010, Volume 28, Issue 25 to December 2010, Volume 29, Issue 5
European Journal of Pain	September 2010, Volume 14, Issue 8 to December 2010, Volume 15, Issue 2.
Urologic Oncology	September 2010, Volume 28, Issue 5 to December 2010, Volume 29, Issue 1.
International Journal of Urology	September 2010, Volume 17, Issue 9 to December 2010, Volume 18, Issue 2.
British Journal of Cancer	September 2010, Volume 103, Issue 5 to December 2010, Volume 104, Issue 4.
Urology	September 2010, Volume 76, Issue 3 to December 2010, Volume 77, Issue 2.
Cancer	September 2010, Volume 116, Issue 17 to December 2010, Volume 117, Issue 4.

I also conducted comprehensive hand searches of my personal files and other relevant papers not identified electronically to increase the likelihood of identifying relevant articles published in journals not indexed electronically.

3.3.4. Study Selection

Study selection followed an iterative process that began with collating, reading and critically appraising all the abstracts identified by the electronic, reference list and hand searches.

- If it was possible to confirm from the abstract alone that an article did not meet the inclusion criteria, it was immediately rejected.
- If an article appeared to fulfil some but not all of the inclusion criteria, or was difficult to accurately assess through the abstract alone, the full text article was retrieved for further analysis.
- Articles that appeared to meet all of the inclusion criteria were also retrieved in full for further analysis.
- If a study appeared acceptable for inclusion but lacked specific information, I contacted the article's authors to request the missing data. If this was ineffective or not possible, the investigation was excluded from entry into the meta-analysis.

All of the retrieved full text articles were then read and analysed in full to determine which studies were acceptable for inclusion into the meta-analysis.

A key component of systematic review methodology is the objective assessment and scoring of the quality of each identified paper. Unfortunately there is no consistent mechanism or gold standard for assessing quality in the predominately cross-sectional studies making up this review that is equivalent to the Cochrane grading system that is used for clinical trials. As a consequence it was very difficult to have any consistent and consensus-based quality assessments in the papers I identified. I was aware of the work by Von Elm and colleagues and the development of the STROBE criteria (Von Elm et al., 2010) but I am also aware that this quality assessment tool has not been widely used and has in some cases been shown to represent a poor marker of quality.

However, it was fundamental to ensure that each of the papers entered into the review were methodologically robust in terms of what and who they were measuring. More specifically, for a study to be entered into the review, it had to provide valid and reliable measures of depression and anxiety, include only biopsy confirmed PCa patients, specifically stipulate what stage of treatment the patients were at during the time of assessment for depression and anxiety and be published in peer reviewed journals. Through the application of these criteria I was able to objectively ensure that each of the studies provided high quality data that would allow me to address my research aim (i.e. the meta-analytical assessment of depression and anxiety prevalence specifically in a PCa) in a valid and reliable manner.

3.3.5. Data Extraction

Data Extraction Process

Extraction of data from studies meeting the inclusion criteria for entry into the meta-analysis was initially undertaken by myself. To test the consistency of my data extraction across the studies, two independent researchers (SE and LL) were recruited to extract data from 6 of the articles included into the meta-analysis. All three researchers involved in the data extraction process then compared the results of their extraction. A points system was utilised to allow for the objective assessment of consistency: 1 point was allocated for variables with identical data extraction and 0 points for variables with differences. This allowed me to determine the

percentage agreement of data extraction across the studies to provide a numerical indicator of consistency. Across the 6 articles, consistency ranged from 92% to 96% (median: 92%).

Piloting

Prior to data extraction, it was necessary to pilot the extraction process to allow for the assessment and identification of which data was required from the extraction process:

- Initially, 10 of the articles meeting the inclusion criteria for entry into the meta-analysis were selected.
- Each article was then individually assessed and key fields of data identified.
- A first draft of the data extraction form, created in an Excel spread sheet (Microsoft, Redmond, WA), was created.
- Extracted data from the first article was then entered into the spread sheet.
- Data extracted from the second article was then entered into the spread sheet. If additional fields of data were identified in the second article, additional columns were added to the spread sheet to accommodate these data.
- I then followed an iterative process of adding to the spread sheet as additional fields of relevant data were identified with each subsequent article.
- Once data from each of the initial 10 articles had been extracted and the data extraction spread sheet finalised, the spread sheet was critically assessed by my two PhD supervisors (Prof George Lewith and Dr Geraldine Leydon).
- Any additions to the spread sheet that were deemed necessary following this supervision were included whilst any sections that were deemed superfluous to the data extraction process were removed. The finalised version of the data extraction template was then utilised for data extraction for the remaining articles.

Format of Data Extraction Spread Sheet

Following the piloting process, the following data fields were selected for entry into the data extraction spread sheet: Bibliographic information; Date of data collection; Geographical location; Clarification of aims and objectives; Study design; Participant inclusion and exclusion criteria; Recruitment procedures; Study sample size; Clinical staging of PCa; Participants age; Ethnicity; Time since diagnosis; Economic status; Educations status; Marital status; Co-morbidity; Stage of treatment (pre, on or post-treatment); Treatments categories (type of treatment selected); Questionnaire utilised; Statistical analysis and results.

3.3.6. Statistical analysis

Standard Method of Meta-Analysis Using Proportions.

The initial method of conducting the meta-analysis of the prevalence of depression and anxiety in PCa was based on simple normal approximations to binomial distributions. The initial combination of these results into an overall estimate is based on combining the individual data available from all studies to give a meta-analysis estimate of the percentage of PCa patients experiencing clinically significant levels of depression and anxiety.

Logits of Proportions Method of Meta-Analysis

However, the accuracy of the above method is dependent upon the near normality of the estimates of the proportions. If there is doubt about normality, an alternative method endorsed by Mantel and Haenszel (1959) uses logits of the proportions instead.

These are more normally distributed than the proportions and are defined as follows

- $\text{logit}(p_i) = \log\{p_i/(1-p_i)\}$
- SE_i = Standard Error of $\text{logit}(p_i) = \sqrt{\frac{1}{n_i p_i} + \frac{1}{n_i(1-p_i)}}$

  with weight $w_i = 1/SE_i^2 = n_i p_i(1-p_i)$.

The meta-analysis logit is now given by

- $log\,it(p) = \frac{\sum_{i=1}^{k} w_i\, log\,it(p_i)}{\sum_{i=1}^{k} w_i}$ with variance = $\text{Var}(\text{logit}(p)) = \frac{1}{\sum_{i=1}^{k} w_i}$.

This is used to produce a 95% confidence interval for logit(p)using $\text{logit}(p) \pm 2\sqrt{\frac{1}{\sum_{i=1}^{k} w_i}}$.

The meta-analysis estimate and confidence limits are then back transformed using

- $p = \frac{exp(log\,it(p))}{1+exp(log\,it(p))}$.

As the initial analysis revealed poor normality, the logits of proportions method of conducting the statistical analyses was decided upon.

Test of heterogeneity.

Cochran's Q test applied to the logits tests the hypothesis of homogeneity of the within study estimates of the proportions, or the logits if preferred.

The test statistic is $Q = \sum_{i=1}^{k} w_i \left[log\, it(p_i) - log\, it(p) \right]^2$ which has a chi-squared distribution with (k-1) degrees of freedom if the estimates are homogeneous. Large values suggest that the estimates are not homogeneous.

3.4. Results

3.4.1. Identified Research Literature

Electronic Database Search Results

The electronic database searches initially yielded 1778 journal article references. 1655 of these were subsequently removed due to either duplication or a clear failure to meet the pre-specified inclusion criteria.

Full text articles were then retrieved and critically appraised for the remaining 123 journal references. Of these, 82 articles were subsequently removed from the review following analysis as they failed to meet key components of the inclusion criteria. The predominant reason for this was that they failed to utilise an acceptable questionnaire to measure depression and anxiety as assessed against my previously conducted questionnaire analysis (see 3.2.2 above).

The remaining 41 articles were then subjected to a second round of analysis which revealed that an additional 15 studies failed to meet the demands of the inclusion criteria. The reasons for the rejection of these final 15 studies included:

- Studies grouping together depression and anxiety scores for both PCa patients and their partners without providing data specifically for the patients (n=3)
- Studies that measured depression and anxiety in a mixed cancer population that included PCa patients but failed to provide data specifically for the PCa sample (n=4)

- Studies that measured depression and anxiety in PCa patients but failed to provide prevalence data in a percentage format or in a format that allowed for the calculation of percentage (n=7)
- Studies that measured depression and anxiety in post-treatment PCa patients that failed to provide information on how long ago treatment ended (n=1)

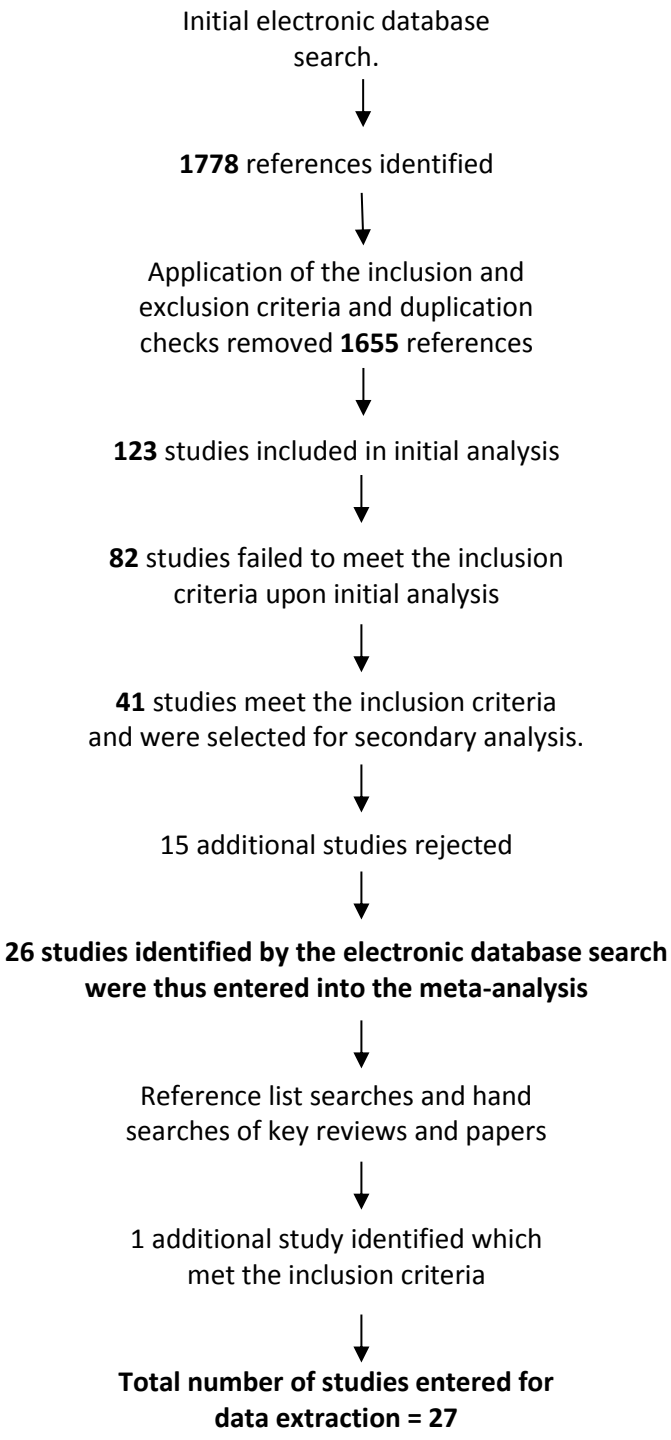
In all cases, the authors of these studies were contacted by email and asked to provide the missing information to allow their study to be entered into the review. In all cases the authors stated that the requested information had not been recorded during the investigation and/or was not available or they failed to respond to my emails.

The remaining 26 articles were subsequently entered into the meta-analysis for data extraction (Figure 1 below).

Reference List and Hand Searches

Hand searches of the key journals identified by the electronic database search revealed no additional journal articles. Searching the reference lists of articles identified through the electronic database search identified 2 journal article references of interest that had otherwise been missed. Full text articles were retrieved for these 2 references, one of which failed to meet the inclusion criteria and was rejected from entry into the meta-analysis. The remaining article met the inclusion criteria and was subsequently entered into the meta-analysis for data extraction. Including this article and the 26 articles identified though the electronic database searches, the total number of studies entered into the meta-analysis numbered 27. A flow diagram of the journal article search process can be seen in Figure 1.

Figure 1: Meta-Analysis Search Overview



3.4.2. Study Characteristics

The following provides an overview of the characteristics of the studies entered into the current meta-analysis both collectively for all 27 studies and, were relevant, as a function of treatment stage (pre-treatment, on-treatment and post-treatment). The key features of each of the studies entered into the review can be seen in Table 3.

Table 3: Key features of the included studies

Author	Year	Sample size	Participant Age	Study Design	Instruments Used	Cancer stage	Treatment stage
Ene	2006	123	63.1	Prospective Longitudinal study	HADS	No data provided	Pre to Post-treatment
Pirl	2008	50	62	Prospective Longitudinal study	BDI	Advanced	Pre and On-treatment
Sharpley	2007	195	69.2	Cross sectional	SDS and SAS	Localised	Post-treatment
Bisson	2002	83	64.5	Prospective Longitudinal study	HADS	Mixed	Pre-treatment
Dirkson	2009	51	73.4	Cross sectional	CES-D	Mixed	On-treatment
Dale	2009	67	67.9	Prospective Cohort Study	HADS MAX-PC	No data provided	Pre-treatment (but all participants had received prior primary therapy)
Gabershagen	2007	115	64.1	Cross sectional	HADS	Localised	Pre-treatment
Gabershagen	2009	84	62.8	Prospective Longitudinal study	HADS	Mixed	Pre-treatment to post-treatment
Hervouet	2005	861	67.9	Cross sectional	HADS	Mixed	Post-treatment
Monga	1999	36	66	Prospective Longitudinal study	BDI	Localised	Pre-treatment to On-treatment to Post treatment
Monga	2005	40	67.8	Longitudinal	BDI	Localised	Pre-treatment to On-treatment to Post-treatment
Pirl	2002	45	69.4	Cross sectional	BDI	Localised and Metastatic	On-treatment
Savard	2005	327	66	Cross sectional	HADS	localised	Post-treatment
Stone	2000	62	69	Longitudinal	HADS	Mixed	On-treatment
Soloway	2004	103	62	Cross sectional	BDI	No data provided	Pre-treatment
Steineck	2002	326	64.5	Cross sectional	CES-D STAI	Localised	Post-treatment
Symon	2006	50	59.9	Longitudinal	HADS	Localised	Pre-treatment to Post-

							treatment
Sharpley	2007	183	69.2	Cross sectional	SDA, SAS	Localised	Post-treatment
Sharpley	2009	150	69.8	Cross sectional	SDS, SAS	Localised	Post-treatment
van Tol-Geerdink	2006	118	70	Longitudinal	HADS	Localised	Pre-treatment
Van den Berg	2009	129	64.9	Cross sectional	CES-D, STAI, MAX-PC	Localised	On-treatment (active surveillance)
Van den Berg	2010	129	64.6	Longitudinal	CES-D, STAI, MAX-PC	Localised	On-treatment (active surveillance)
Monga	2001	40	67.6	Longitudinal	BDI	Localised	Pre-treatment to Post-treatment
Korfage	2006	299	65.4	Longitudinal	HADS, STAI	Mixed	Pre-Post treatment
Bitsika	2009	381	No data	Cross sectional	SDS, SAS	Localised	Post-treatment
Nordin	2001	118	No data	Longitudinal	HADS	Localised & Advanced	Pre-treatment
Burnet	2007	329	68.8	Prospective Longitudinal study	HADS	Localised	On and post-treatment

Study Locations

The geographical locations of the included studies varied widely with the majority originating from America. Of the 27 studies entered into the review, 9 were conducted within America, 4 in both Australia and Holland, 3 in the United Kingdom, 2 each in Sweden, Germany and Canada and 1 in Finland

Study Sample Sizes

The samples sizes of the studies entered into the review varied widely from 36 to 861. The total sample size across all 27 studies was 4494 with a mean sample size of 158. The sample sizes of the individual treatment stage groups (pre, on and post-treatment) can be seen in Table 4. N.B. The collective total sample size of these three groups exceeded the total of the collective 27 studies entered into the review as several longitudinal studies reported data for two or more of the three groups (i.e. both pre-treatment and on-treatment data were reported for the same sample of patients).

Participant Age

Data on participant age was reported by 24 of the 27 studies and in all 24 cases mean age was reported. The range of mean ages across the 24 studies varied from 57.5 years to 73.2 years.

The mean age of all participants from these 24 studies was 66.3 years (3.3). Three studies failed to report participant age in any format. The mean age of the participants in each of the three treatment groups can be seen in Table 4.

Cancer Staging

Data regarding participant cancer stage was reported by 23 of the 27 studies. There was a general lack of consistency regarding reporting methods. Several studies utilised the clinical T-staging system of T1 (localised) to T4 (metastatic) whilst the majority simply graded PCa as localised, advanced or metastatic. No study reported patient disease stage using the tumour-nodes-metastasis (TNM) system which has been internationally recommended to promote consistency (Kirby & Taylor, 2008). The majority of patients had been diagnosed with localised disease (n=3270), followed by advanced (513) and metastatic PCa (87), as shown in Table 4 below.

Table 4: Overview of Study Sample Sizes and Participant Age

	All studies	Pre-Treatment Studies	On-Treatment Studies	Post-Treatment Studies
Study Sample Sizes	4494	1707	723	3087
Participant Ages	66.3 (3.3)	64.8 (2.9)	67.6 (3.3)	66.9 (2.4)
Number of patients with localised PCa	3270	1299	563	2236
Number of patients with advanced PCa	513	162	72	441
Number of patients with metastatic PCa	87	58	40	7

Cancer Treatments Undertaken

Radical treatment options for PCa include radical prostatectomy, radiotherapy, hormone therapy and chemotherapy whilst passive treatments include active surveillance and watchful waiting. All of these treatment modalities were utilised within the 27 studies entered into the review in varying degrees. Four studies grouped on-treatment patients together. This made it impossible to classify these patients into specific treatment categories. It is for this reason that the total number of men listed in each treatment category does not equal the total sample size of 4494. Table 5 below provides an overview of the number of participants undergoing each of the treatment options. Unfortunately, it was not possible to stratify the treatments undertaken as a function of either disease stage (localised, advanced or metastatic) or

treatment stage (on-treatment or post-treatment). Thus the data in Table 5 provides a collective overview of the treatments undertaken by all of the patients, irrespective of disease or treatment stage. Additionally, several of the "pre-treatment" studies recruited participants who had yet to decide upon treatment. Such patients are listed in Table 5 as 'newly diagnosed'.

Table 5. The number of PCa patients undertaking each treatment modality

Radical Prostatectomy	Radiotherapy (EBRT & Brachytherapy)	Hormone Therapy (orchiectomy and ADT)	Chemotherapy	Active Surveillance or Watchful Waiting	Newly diagnosed (no treatment yet selected)
924	1578	264	24	418	304

Questionnaires Analysis

Of the 12 questionnaires meeting the questionnaire inclusion criteria as listed in section 3.2.2, only 7 were utilised by the 27 studies entered into this meta-analysis. Table 6 lists the 7 questionnaires, the frequency with which they were used and the clinical cut-off scores utilised to define depression and anxiety caseness.

Table 6. Questionnaires utilised , frequency of use and cut-off scores utilized

Questionnaire Name	**Frequency of Use**	**Clinical Cut-Off Scores Utilised**
Hospital Anxiety and Depression Scale (HADS)	13	HADS-A: ≥8 HADS-D: ≥8
Beck Depression Inventory (BDI)	6	≥10
Self Rating Anxiety Scale (SAS)	4	≥36
Self Rating Depression Scale (SDS)	4	≥40
Centre for Epidemiologic Studies Depression Scale (CES-D)	4	≥15
Stait-Trait Anxiety Scale (STAI)	4	≥44
Memorial Anxiety Scale for Prostate Cancer (MAX-PC)	3	≥27

3.4.3. Meta-Analyses

Assessment of Homogeneity

Inevitably, any group of studies brought together into a review will differ. It was important to accurately measure and define this heterogeneity to ensure that the results found in the individual studies are similar enough to be confident that the combined estimate will be a meaningful description of the entire data set.

Cochran's Q test was applied to the logits transformations to test for heterogeneity across the studies, with large Q waves suggesting that the prevalence estimates are not homogeneous. The analysis of the included studies found that the Cochran Q values varied between Q= 1.7 and Q=256.7, suggesting there was a degree of heterogeneity among the studies.

There are likely to be many reasons for this variability which include differing sample sizes, selective populations and the differing instruments that have been used to measure depression and anxiety.

Despite the considerable variation amongst the estimates reported in the literature, as confirmed by the large Q values, for completeness, and based on the advice of my statistical supervisor, the meta-analysis results have been provided even for those cases where heterogeneity was evident.

Meta-Analysis of Depression Prevalence Number of studies reporting depression

26 of the 27 studies reported data on depression prevalence. Of these 26, 13 reported depression in pre-treatment patients, 10 in on-treatment patients and 13 in post-treatment patients. N.B. The number of total studies from the 3 groups exceeded 26 as several longitudinal studies reported depression in multiple treatment groups (i.e. in both pre-treatment and on-treatment groups)

Number of Patients Measured for Depression

1259 participants provided measures of depression in the pre-treatment group, 723 in the on-treatment group and 3157 in the post treatment group.

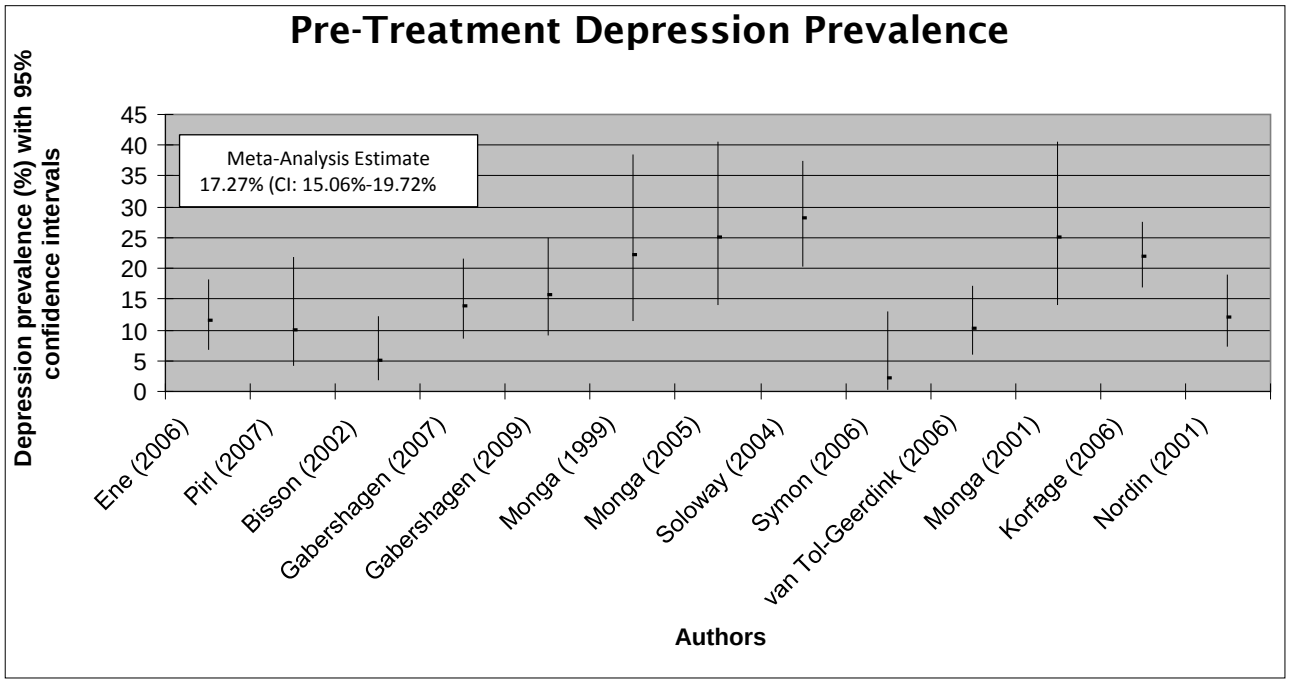
Depression Prevalence

The following provides an overview of the prevalence of depression for each of the three treatment groups (pre, on and post-treatment). The meta-analysis statistical outputs for each of the analyses can be seen in Appendices 2-4.

3.3.4.1. Pre-Treatment Depression

Across the 13 studies that provided measures of depression in PCa patients prior to undergoing treatment (see Figure 2), the prevalence of depression was 17.27% (CI: 15.06%-19.72%). Within these 13 studies, 6 studies provided measures of depression specifically in men with localised PCa. For this sub-group, the prevalence of depression was 16.25% (CI: 12.65%-20.63%).

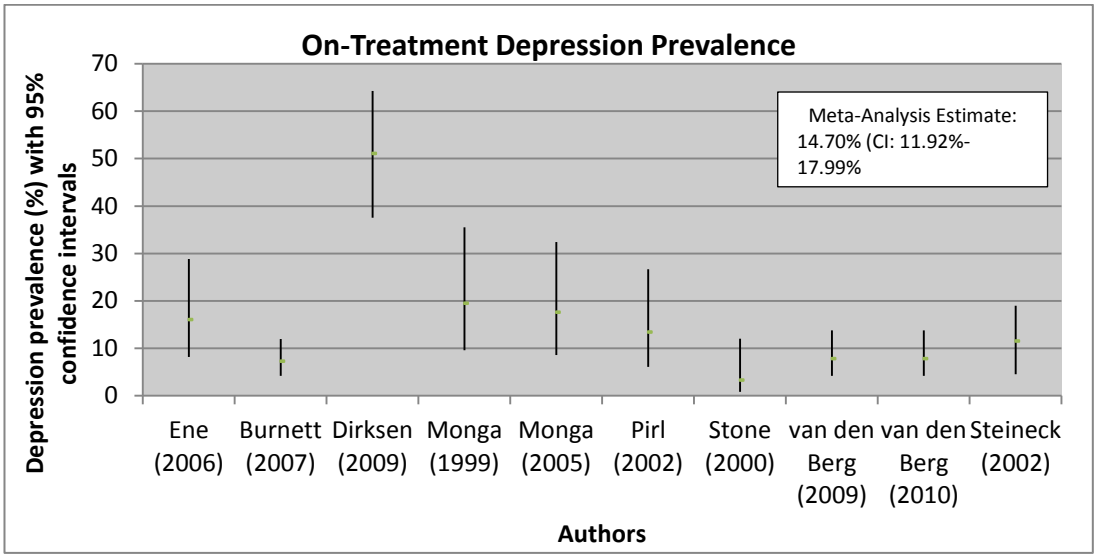
Figure 2: Prevalence of depression in pre-treatment studies. Point estimates with 95% confidence intervals.



3.3.4.2. On-Treatment Depression

Across the 10 studies that provided measures of depression in PCa patients currently undergoing treatment (see Figure 3), the prevalence of depression was 14.70% (CI: 11.92%-17.99%). Within these 10 studies, 5 studies provided measures of depression specifically in men with localised PCa. For this sub-group, the prevalence of depression was 10.70% (CI: 7.31%-12.76%).

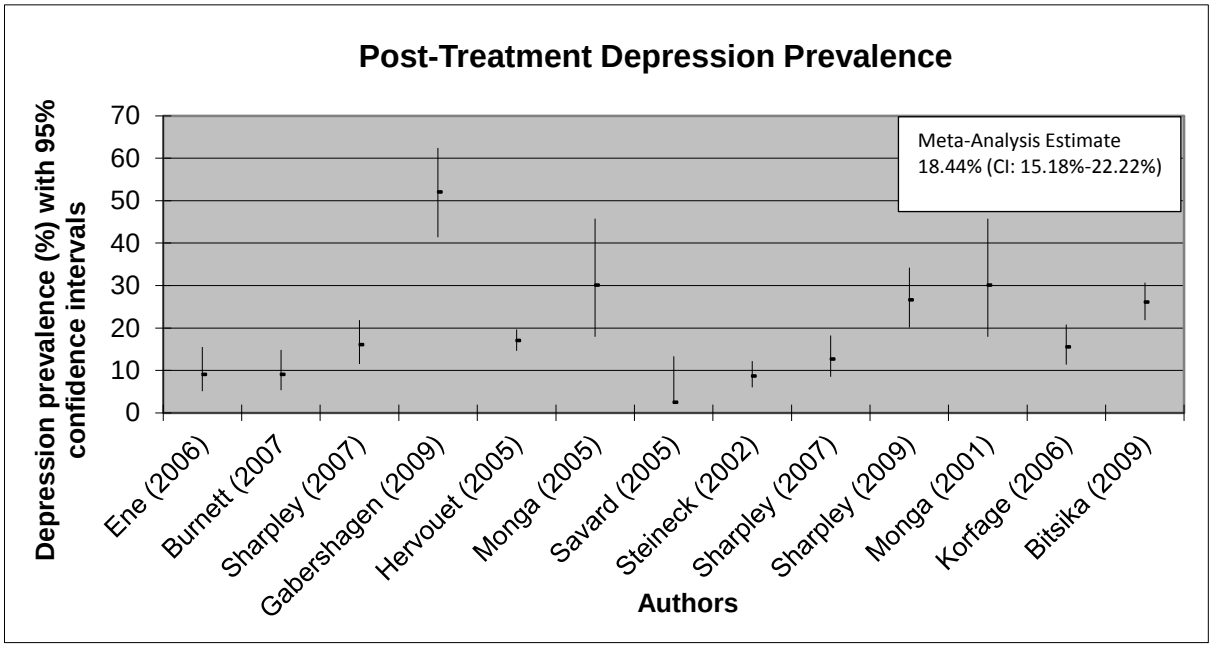
Figure 3: Prevalence of depression in on-treatment studies. Point estimates with 95% confidence intervals.



3.3.4.3. Post-Treatment Depression

Across the 13 studies that provided measures of depression in PCa patients who had completed treatment (see Figure 4 below), the prevalence of depression was 18.44% (CI: 15.18%-22.22%). Within these 13 studies, 8 studies provided measures of depression specifically in men with localised PCa. For this sub-group, the prevalence of depression was 19.25% (CI: 15.58%-23.15%).

Figure 4: Prevalence of depression in post-treatment studies. Point estimates with 95% confidence intervals



3.4.4. Meta-Analysis of Anxiety Prevalence

Number of studies reporting anxiety

20 of the 27 studies reported data on anxiety prevalence. Of these 20, 9 reported anxiety in pre-treatment patients, 4 in on-treatment patients and 11 in post-treatment patients. N.B. The number of total studies from the 3 groups exceeded 20 as several longitudinal studies reported anxiety in multiple treatment groups (i.e. in both pre-treatment and on-treatment groups)

Number of Patients Measured for Anxiety

1057 participants provided measures of anxiety in the pre-treatment group, 501 in the on-treatment group and 3077 in the post-treatment group.

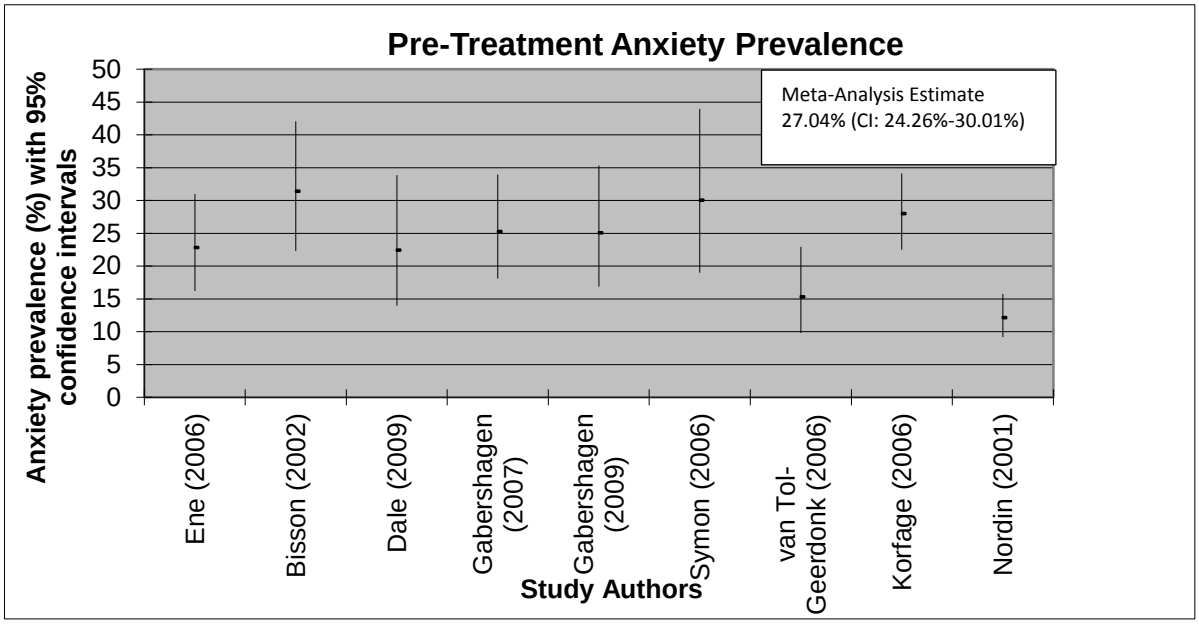
Anxiety Prevalence

The following provides an overview of the prevalence of anxiety for each of the three treatment groups (pre, on and post-treatment). The meta-analysis statistical outputs for each of these analyses can be seen in Appendices 5-7.

Pre-Treatment Anxiety

Across the 9 studies that provided measures of anxiety in PCa patients prior to undergoing treatment (see Figure 5), the prevalence of anxiety was 27.04% (CI: 24.26%-30.01%). Within these 9 studies, 6 studies provided measures of anxiety specifically in men with localised PCa. For this sub-group, the prevalence of anxiety was 25.52% (CI: 17.85%-27.98%).

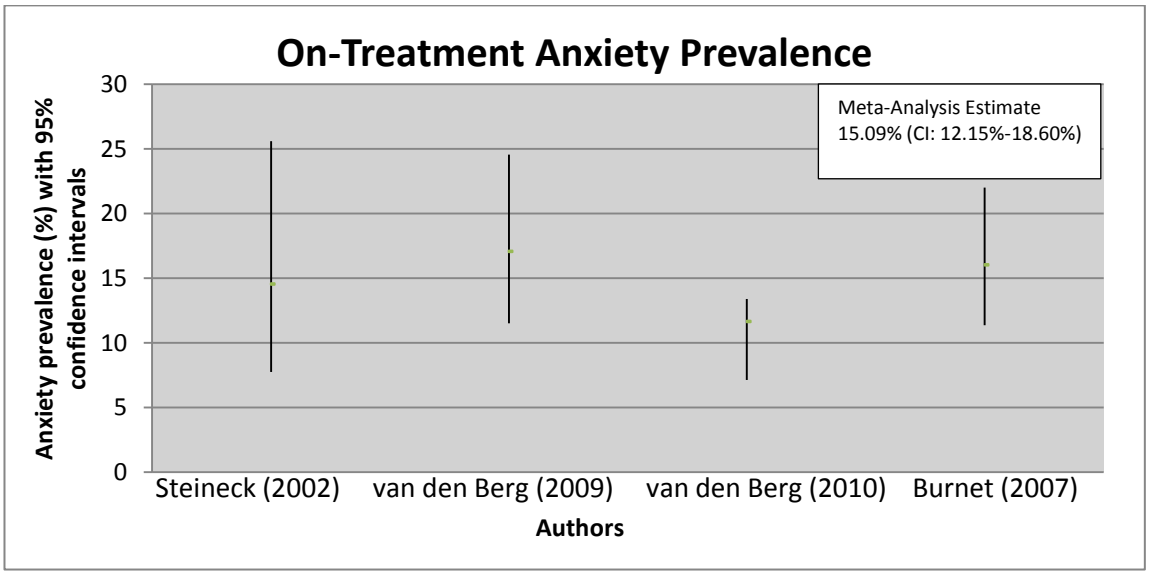
Figure 5: Prevalence of anxiety in pre-treatment studies. Point estimates with 95% confidence intervals.



3.3.6.2. On-Treatment Anxiety

Across the 4 studies that provided measures of anxiety in PCa patients currently undergoing treatment (see Figure 6), the prevalence of anxiety was 15.09% (CI: 12.15%-18.60%). Within these 4 studies, 3 studies provided measures of anxiety specifically in men with localised PCa. For this sub-group, the prevalence of anxiety was 15.17% (CI: 12.04%-18.95%).

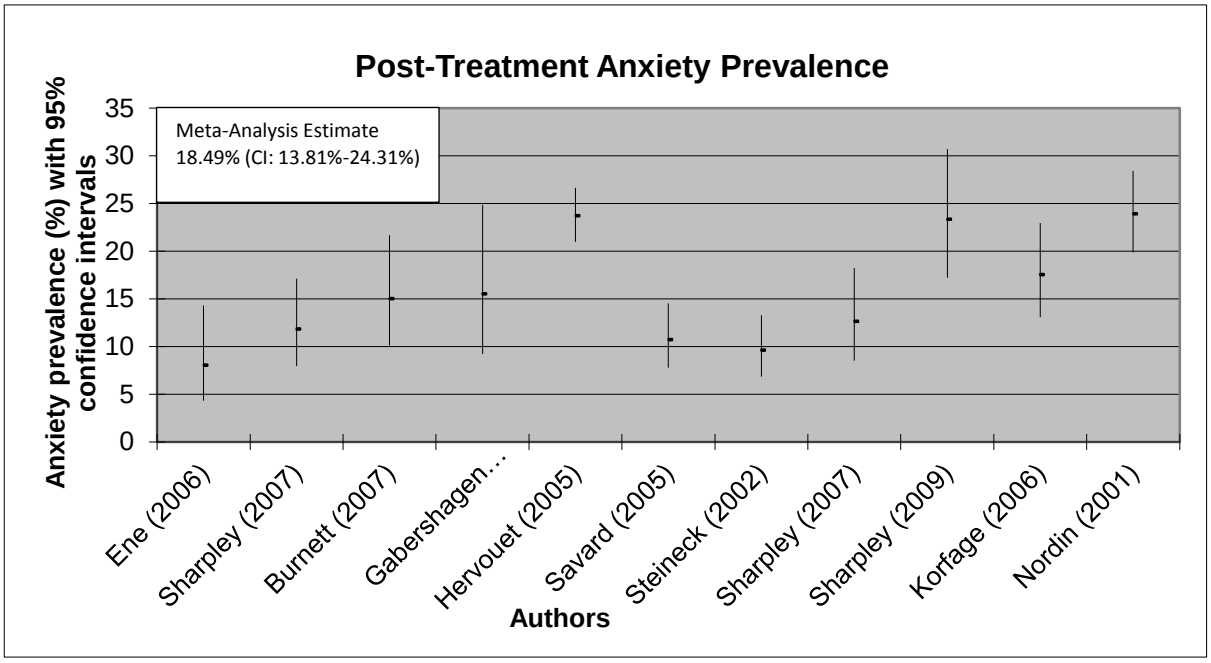
Figure 6: Prevalence of anxiety in on-treatment studies. Point estimates with 95% confidence intervals.



3.3.6.3. Post-Treatment Anxiety

Across the 11 studies that provided measures of anxiety in PCa patients who had completed treatment (see Figure 7), the prevalence of anxiety was 18.49% (CI: 13.81%-24.31%). Within these 11 studies, 10 studies provided measures of anxiety specifically in men with localised PCa. For this sub-group, the prevalence of anxiety was 18.81% (CI: 14.06%-24.70%).

Figure 7: Prevalence of anxiety in post-treatment studies. Point estimates with 95% confidence intervals.

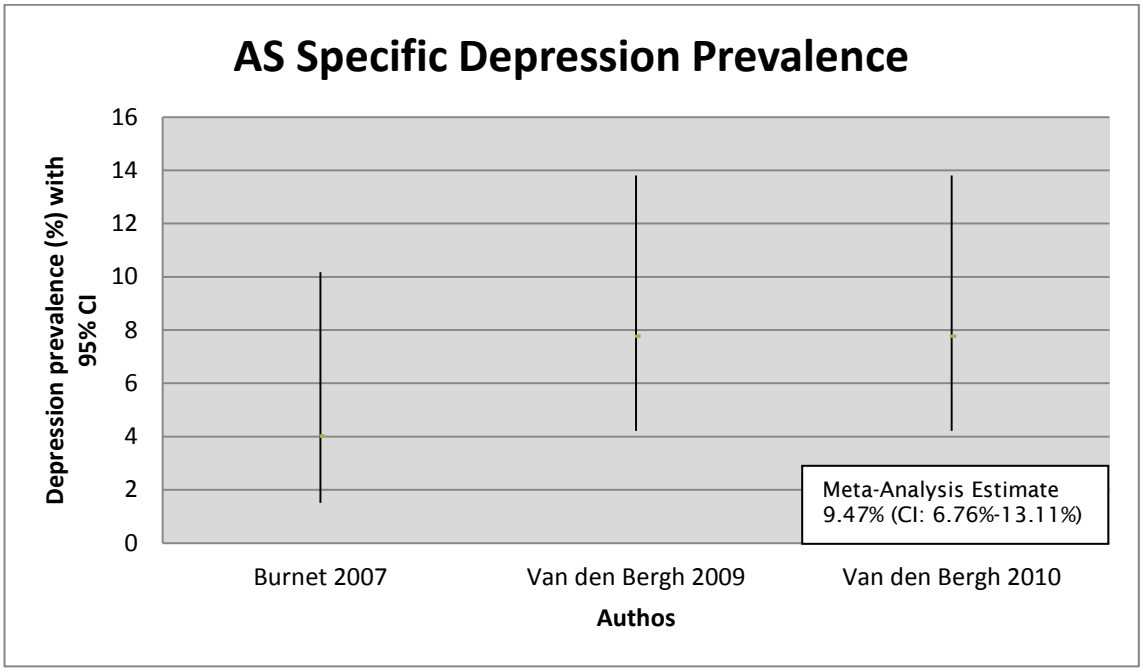


Depression and Anxiety Prevalence with Active Surveillance Patients

3.3.6.4. Active Surveillance Specific Depression Prevalence

3 studies provided measures of depression in PCa patients being managed with AS (see Figure 8). Across these 3 studies the prevalence of depression was 9.47% (CI: 6.76%-13.11%).

Figure 8: Prevalence of depression in PCa patients being managed with AS. Point estimates with 95% Confidence intervals

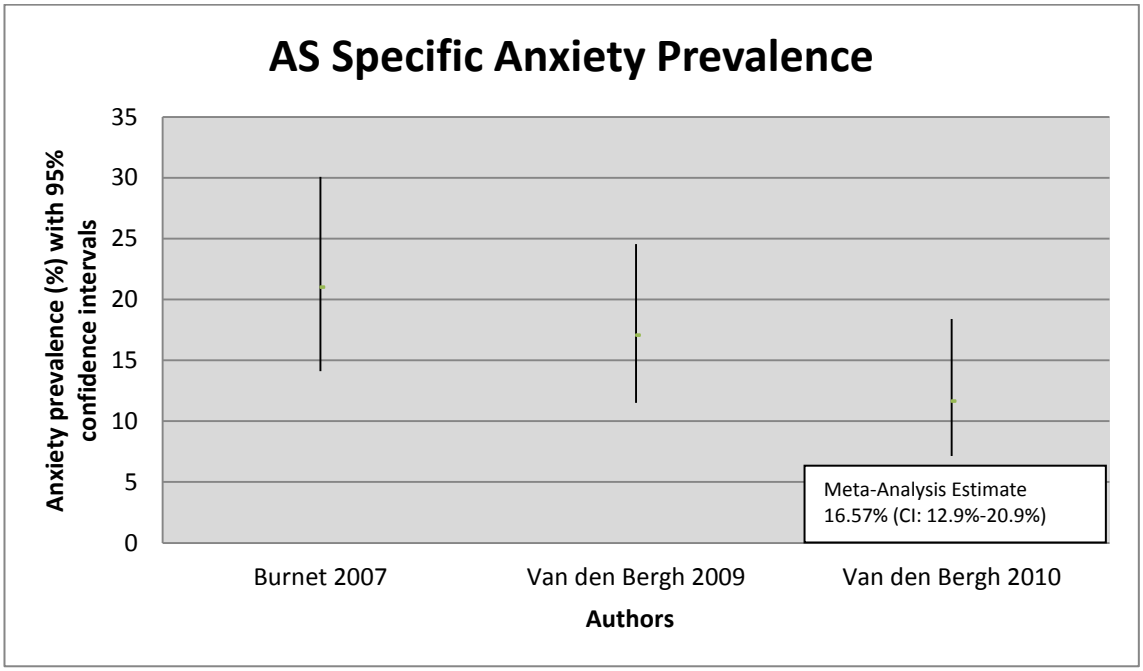


3.3.6.5. Active Surveillance Specific Anxiety Prevalence

3 studies provided measures of anxiety in PCa patients being managed with AS (see Figure 9).

Across these 3 studies the prevalence of anxiety was 16.57% (CI: 12.96%-20.95%).

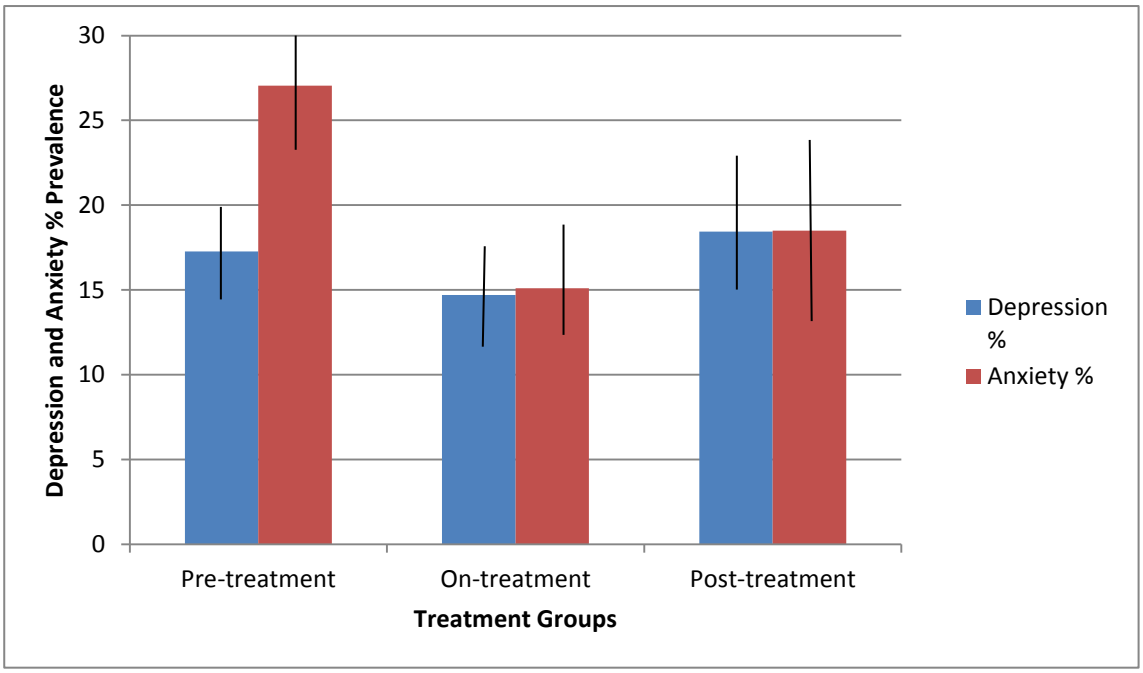
Figure 9: Prevalence of anxiety in PCa patients being managed with AS. Point estimates with 95% Confidence intervals



Depression and Anxiety Prevalence Across and Within Treatment Groups

Figure 10 below provides a pictorial representation of the prevalence of depression and anxiety both within and across each of the three treatment groups.

Figure 10: Prevalence of depression and anxiety within and across the three treatment groups.



3.5. Discussion

3.5.1. Key Findings

The findings of the current meta-analysis suggest that over the trajectory of the PCa journey, depression and anxiety prevalence are highest in patients who have yet to undergo treatment (17.27% and 27.4% respectively), lowest in patients who are currently undertaking treatment (14.70% and 15.09% respectively) before rising again in patients who have completed treatment (18.44% and 18.49% respectively). The relatively small variation and consequently tight 95% confidence intervals observed within these prevalence rates across the different treatment stages, along with the large collective sample size of the meta-analysis (n=4494) suggests these conclusions are valid and robust summaries of the sample of patients surveyed.

There is a real need within the clinical management of PCa, particularly as the burden of this chronic disease is escalating with the increasing uptake of PSA screening and improved diagnosis and treatment, for an increased awareness of the issue of psychological distress

among men diagnosed with, being treated for and surviving through a PCa diagnosis. The results of the current meta-analysis go some way in addressing this issue by providing those working within the field of PCa with an overview of the likely prevalence of depression and anxiety in the patients they treat over the trajectory of the treatment journey.

With additional epidemiological investigation it is hoped that these results will help those involved in the treatment of PCa to offer a more "risk adapted" approach to the management of psychological distress for PCa patients. This will allow for the provision of more intensive screening and support to individuals who are most at risk of psychological morbidity based upon their current stage of treatment.

Likewise, this review has also produced a range of depression and anxiety prevalence data which can be compared with the prevalence rates obtained for depression and anxiety specifically for AS patients (Chapter 4) to help determine whether men on AS experience a greater or lesser risk of depression and anxiety than other PCa patients .

3.5.2. Key Findings: Pre, On and Post-Treatment Depression Prevalence

The results pertaining to the prevalence of depression in the pre-treatment PCa patients was very much in keeping with that recorded from multiple cancer populations who have been shown to typically experience a depression prevalence of between 15%-22% (Kugaya et al., 2000; Wong-Kim & Bloom, 2005). These data suggest that in newly diagnosed PCa patients, the rates of depression are very similar to that observed in patients across the cancer site spectrum.

However, is it important to highlight that depression prevalence within the pre-treatment category may have been heavily skewed by the proportion of recruited participants with localised PCa versus those with metastatic disease. Of the 13 studies that reported measures of depression in patients prior to treatment, 1299 participants with localised disease were recruited in comparison to only 58 with metastatic disease. In contrast, much of the research into depression in breast and lung cancer has included large cohorts of patients with metastatic disease (Lo et al., 2010; Giese-Davis et al., 2006). Given that most men with localised PCa are asymptomatic, or at worst suffering from only mild symptoms, one would reasonably expect depression prevalence to be significantly lower within such patients in comparison to those diagnosed with metastatic disease who typically experience substantially higher levels of physical dysfunction (Taylor & Kirby, 2008).

Additionally, research suggests that in PCa patients who have yet to undergo treatment, pain is one of the most accurate predictors of depression (Garbershagen et al., 2008). Given than metastatic PCa is associated with a great deal of pain (Bader et al., 2010), particularly skeletal pain (Drudge-Coates, 2006), it is possible that had a larger cohort of men with metastatic PCa been included within this review, the prevalence of depression would have been significantly greater.

It is of interest that the results of the current meta-analysis suggest that PCa patients undergoing treatment (on-treatment group) experienced a reduction in depression in comparison to that observed in pre-treatment PCa patients. Whilst this reduction may have lacked statistical significance (a 2.17% reduction), it is still of clinical interest as much generic cancer research suggests that the initiation of radical treatment is characterised by an increase in psychological distress and depressive symptomology (Ahles & Saykin, 2008; Sharifi, Gulley & Dahut, 2005).

Relating specifically to PCa, the initiation of radical treatment has been linked to substantial reductions in health related quality of life as men face the prospect of temporary, and in some cases permanent impairments to sexual, urinary and bowel function (Couper et al., 2006; Ames, Winston & Ames, 2008). Given the widely reported relationship between declining quality of life and the onset of depression in multiple site cancer populations (Avis, Crawford & Manuel, 2005; Redekner, Lev & Ruggiero, 2000), one could reasonably expect depression prevalence to increase during treatment, a pattern that has been shown to exist in some other cancers (Redekner, Lev & Ruggiero, 2000; Holmes & Williamson, 2008).

However, the results of the current meta-analysis suggest the opposite to be true in that PCa patients experienced a small and insignificant reduction in depression whilst undergoing treatment. Whilst few would argue against the distressing physical side effects associated with PCa treatment, it would appear that such side effects, whilst negatively impacting upon overall quality of life (Lev et al., 2009; Monga et al., 2005) do little to induce depressive symptomology.

However, caution must be taken when interpreting these results for several reasons. Firstly, a large proportion of the results were obtained from cross sectional studies. Of the 10 studies that recorded depression in on-treatment patients, 5 were longitudinal and 4 were cross sectional in design. However, the cross sectional studies recruited substantially more participants than their longitudinal counterparts (554 versus 317, respectively).

The majority of PCa treatments are long term interventions. Radiotherapy is typically administered over 6-8 months whilst PCa patients can remain on hormone therapy indefinitely (Kirby & Taylor, 2008). If the depression inducing nature of such treatments are to be better understood, longitudinal studies would be much better suited to the task as they would allow for the more accurate assessment of the altering psychological health of the patient over the course of their treatment. The predominant use of cross-sectional data collection means it is very difficult to create real comparisons regarding how the prevalence of depressive symptomology may have changed over the course of treatment. It would be beneficial for future longitudinal studies to address this issue.

Furthermore only 10 studies provided validated measures of depression in PCa patients undergoing treatment, compromising 871 participants. This represents a relatively small sample size that may not adequately reflect the true relationship of the depression inducing nature of PCa treatment. Furthermore, of these 871 participants, only 40 had received a diagnosis of metastatic PCa. Thus another possible explanation for the reduction in depression observed in this cohort of patients was that over 96% of them were diagnosed with localised disease. Given that depression is more commonly induced by long term fears and concerns, such as survival and cancer spread, it is possible that the lower rate of depression observed was a factor of the high percentage of men living with localised PCa who had received a highly favourable prognosis.

The results of the meta-analysis highlighted post-treatment depression prevalence to be the highest of the three treatment stages at 18.44%. This represents an almost 4% increase in depression in comparison to that observed in patients undergoing treatment. In the absence of any comparable data, it is difficult to explain the possible factors relating to this rise in post-treatment depression.

One possible explanation may lie in the longevity of the associated side effects of PCa treatment. The sexual, urinary and bowel dysfunction commonly induced by hormone therapy and radiotherapy can be long lasting and in some cases permanent (Kirby & Taylor, 2008). Similarly, even with the increased utilisation of nerve sparing techniques, radical prostatectomy is still associated with a 50% and 30% chance of long term impotence and incontinence, respectively (Kirby & Taylor, 2008). It is possible that a majority of the post-treatment men reviewed within this meta-analysis were still experiencing substantial physiological side effects in the months and years after the completion of treatment, a factor that may help explain the increased depression prevalence observed.

Unfortunately the majority of the studies entered into this meta-analysis recorded depression prevalence in post-treatment PCa patients without stratifying the results as a function of the specific treatments undertaken. Whilst such research has allowed for the accurate assessment of depression in generic PCa patients who have completed treatment, it does little to further our knowledge of how individual treatment options may increase or decrease a patient's predisposition to psychological morbidity.

Each of the treatments for PCa (surgery, hormone therapy, radiotherapy and active surveillance) are associated with varying and unique physical and psychological side effects. It would be beneficial to the understanding of the management of this disease if we could identify which treatment options, if any, increase the risk of depressive symptomology. The speed and pattern of PCa progression has been shown to be remarkably similar irrespective of the treatment options undertaken (Kirby & Taylor, 2008). If specific treatments are shown to increase the chances of developing post-treatment depression, such knowledge could be beneficial to both clinicians and patients in helping them to select treatments that maximise survival but minimise the risk of subsequent psychological morbidity and the reduced quality of life that accompanies it.

3.5.3. Key Findings: Pre, On and Post-Treatment Anxiety Prevalence

It was of interest that pre-treatment anxiety (27.4%) was the single highest prevalence rate observed, for both depression and anxiety, within the meta-analysis. Whilst the anxiety inducing nature of treatment selection across multiple illnesses, including cancer, has been heavily researched (Stark & House, 2002; Stark et al., 2002), the clinical implications of such findings specifically within PCa are important. The growing foundation of research that exists within this area suggests that PCa patients presenting with clinically significant anxiety are prone to select poorer treatment options and experience less overall satisfaction with those choices (Dale et al., 2009; van Tol-Geerdink et al., 2006), resulting in a significant reduction in quality of life and heightened levels of psychological distress.

This finding is of clinical importance. If PCa patients are selecting poorer treatment options as a result of high levels of anxiety, the screening and implementation of interventions to minimise anxiety before treatment selection would appear to be of paramount importance. Were this to be done, it would allow for the more objective assessment of the available treatment options by the patient, a factor that has been shown to increase treatment satisfaction and reduce the level of psychological distress experienced (Dale et al., 2009).

It is also of interest that there were no confounding factors within the sample of PCa patients measured for pre-treatment anxiety that may explain the high levels of anxiety experienced. Metastatic cancer patients have been shown to experience significantly greater levels of anxiety in comparison to those diagnosed with localised disease (Stark et al., 2002). Yet within the current meta-analysis, only 44 out of 1057 participants measured for pre-treatment anxiety had metastatic disease, suggesting that the high anxiety observed was not a factor of disease stage.

Similarly, age has also been shown to be a key factor relating to anxiety in PCa. Younger men have been shown to experience significantly higher levels of anxiety than older men, a relationship that appears to be heavily rooted in fears about the loss of sexual potency (Soloway et al., 2004; Couper et al., 2006). However, the 1057 participants measured for pre-treatment anxiety did not significantly differ in age from the men measured for anxiety in the other treatment categories. This suggests that age was not a significant factor relating to the high prevalence rate observed. In the absence of any such confounding factors, it would appear that the high prevalence of clinical anxiety recorded may simply be a factor of the distress inducing nature of a PCa diagnosis and the realisation of the likely physical side effects associated with treatment that the patient will very soon have to face.

A substantial reduction in anxiety prevalence was observed in PCa patients currently undergoing treatment. This reduction mirrors very closely the pattern observed for depression which also saw a reduction in prevalence rates from pre-treatment to on-treatment. It is difficult to postulate why anxiety experienced such a marked reduction in patients currently undergoing treatment. It is possible that cancer patients are most anxious prior to the initiation of treatment as they face the threat of treatment and the associated physical side effects of such treatment, anxiety which then dissipates once the treatment actually begins. This dissipation may be aided by feelings of empowerment, hope or simply the realisation that proactive measures are being taken to treat their disease (Holland, 1998).

It is of note that the sample size of participants measured for anxiety whilst undergoing treatment was the smallest observed within the meta-analysis and was limited to only four studies, made up of 501 participants. Such a sample size is relatively small in comparison to that observed within the other treatment groups making up this meta-analysis and in additional meta-analyses assessing anxiety prevalence in other cancer populations (Rooney, Carson & Grant, 2010; Fann et al., 2008). It is possible that the lower prevalence of anxiety

observed may have been influenced by the limited sample size of participants recruited and measured for on-treatment anxiety.

As observed for depression, anxiety increased in PCa patients who had completed treatment in comparison to those undergoing treatment. With such little additional research with which to compare the findings of the current meta-analysis, it was again difficult to explain these data. However, whilst the heightened levels of depression experienced by post-treatment PCa patients may be attributed to physical side effects, it is more likely that the increased prevalence of anxiety in post-treatment PCa patients was related to fears about cancer recurrence (Harrison, Haddard & Maguire, 1995; Ashby et al., 1996).

Research suggests that whilst undergoing cancer treatment, the majority of psychological distress experienced is a function of the fears and concerns the patient holds regarding treatment related side effects (Stark & House, 2000). However, after the cessation of treatment, the predominant cause of anxiety tends to shift away from the immediate concerns of treatment side effects to longer term fears about recurrence, recovery and survival (Skaali et al., 2009). It is possible that for the post-treatment PCa patients reviewed within this meta-analysis, the increase in observed anxiety may have been precipitated by such fears.

3.5.4. Strengths and Limitations

The current meta-analysis is the first of its kind to provide a rigorous assessment of the prevalence of depression and anxiety in PCa patients across the trajectory of treatment. It was an aim of the review to ensure than only studies specifically measuring depression and anxiety were entered into this review. Doing so has ensured that the generated results provide an accurate estimate of depression and anxiety as individual and unique psychological morbidities. This is in contrast to the majority of the previous research within this area which has recorded generic quality of life indices. Whilst such research is of value, if depression and anxiety with PCa is to be more effectively identified and managed, an initial and robust estimate of prevalence is required. The current meta-analysis has gone some way to achieving this.

However, there are several key limitations to the results generated than need to be addressed when interpreting the clinical relevance of the findings. Firstly, it is likely that the onset of psychological distress in men diagnosed with PCa is not an acute threat that quickly passes but a chronic one with peaks and troughs of severity that vary according to treatment stage and clinical disease progression. These may include the fear of upcoming treatment, treatment

related side effects, fear of progression, actual progression and final transfer to palliative care pathways. Unfortunately the majority of studies entered into the review were cross sectional in design. Such studies did not allow for the assessment of the overall proportion of men who suffer from some degree of psychological distress during their PCa journey, meaning that the overall the numbers of people affected at some stage may be higher than I was able to identify from this analysis. I would need to conduct a sustained longitudinal cohort study to resolve this question.

Likewise, none of the included studies provided any form of data relating to the patients' history of depression and anxiety. Consequently, it was not possible to determine whether a history of depression and anxiety acted as a significant predictor of current depression and anxiety.

Secondly, high levels of heterogeneity were observed in the meta-analyses of both depression and anxiety, suggesting considerable differences in the prevalence estimates across the included studies. Given the high level of variety observed across the included investigations in terms of study sample sizes, the clinical characteristics of the sample (disease stage and treatment type) and the different instruments used for assessing depression and anxiety, this heterogeneity was largely to be expected.

This is particularly true given that whilst all of the questionnaires utilised in this meta-analysis provided valid and reliable measures of anxiety and depression, some of the instruments measured slightly different constructs of these conditions. For example, the MAX-PC provides a valid and reliable measure of anxiety and has shown to be significantly correlated to other gold-standard measures of general anxiety (as assessed against the DSM-IV criteria). Yet the MAX-PC is different to the other instruments utilised in this meta-analysis as it measures anxiety specific to PCa. As a result the MAX-PC assessed a different form of anxiety to the more generalised instruments such as the HADS. This is likely to have impacted upon the data generated and as such needs to be taken into account when interpreting the results of this meta-analysis.

Whilst standard procedures for addressing the levels of heterogeneity observed could have been adopted it was ultimately my decision, in conjunction with advice from my statistical supervisor, to include all eligible investigations into the meta-analysis to provide a more inclusive and complete assessment of depression and anxiety prevalence in PCa. However, this represents an important limitation to the meta-analysis and as such any conclusions drawn from the generated results need to be interpreted with caution.

Furthermore, this study did not compare the depression and anxiety prevalence rates generated directly to that observed in a cohort to healthy men or men with other cancers. As a consequence, we were unable to specifically determine how PCa and its treatment impacted on the prevalence of psychological distress observed. The essentially descriptive nature of this study therefore needs to be noted.

There was also very little detail provided regarding the importance of post-treatment outcomes and subsequent depression and anxiety prevalence. For example, it is possible that depression and anxiety in post-prostatectomy patients would vary substantially depending on factors such as positive or negative margin status. Unfortunately, it was not possible to formally investigate the properties of the populations to determine whether there were any such differences that would explain this variability. This represents an important limitation to the findings of this study. It is important that future studies into the assessment of depression and anxiety in this patient group carefully identify the characteristics of their populations to address this issue.

Lastly, I was not able to determine through the meta-analytical process whether the prevalence of depression and anxiety was a factor of the type of PCa treatment undertaken. The associated side effects of PCa treatment vary widely. For men undergoing radical intervention urinary incontinence, sexual impotence and bowel dysfunction are common (Kirby & Taylor, 2008). For men opting for active surveillance (AS) for slow growing localised PCa, the picture is less clear.

Active surveillance is a treatment approach unique to PCa and involves the withholding of radical intervention in favour of close disease monitoring. However, very little is currently known or understood about the psychological ramifications of being diagnosed with a malignant cancer and being withheld treatment. It has been speculated that living with an "untreated" cancer in this way predisposes PCa patients to a risk of psychological distress (Latini et al., 2007; Pickles et al., 2007; Burnet et al., 2007).

This is an issue of clinical importance. Survival rates for men with PCa are very good. Consequently the optimisation of quality of life over the course of treatment is of paramount importance. If we were able to understand which treatment protocols induce the highest prevalence of distress it may provide a novel avenue in which to streamline the screening and management of depression and anxiety by offering patients undertaking such treatments with early, preventive support prior to and during the treatment process.

One treatment modality in particular that may benefit substantially from such research is AS, due to the uncertainty associated with this treatment approach, the substantial increase in the number of men being managed in this way and the current shortfall of research addressing the psychological ramifications of this treatment approach.

3.5.5. Previous Research

The number of asymptomatic men being diagnosed with slow growing localised PCa is increasing each year in the UK (Cancer Research UK, 2010). The recently updated NICE Clinical Guidelines for PCa (NICE, 2014) recommend AS as the primary treatment approach for such men. Consequently the utilisation and uptake of AS within the UK is increasing (NICE, 2014). Yet the results of the current meta-analysis clearly highlight that the issue of psychological morbidity among these PCa patients is very poorly described, defined and managed.

Only 4 of the 27 studies entered into this review obtained measures of depression and anxiety from PCa patients being managed with AS (Steineck et al., 2002; Burnet et al., 2007; van den Berg et al., 2009; van den Berg et al., 2010). In all cases the sample sizes of these studies were small (n=<129) and had been recruited exclusively from single centres. This has limited the representativeness and generaliseabilty of their findings. This represents a substantial void in our understanding of the management of psychological distress in this burgeoning patient group.

Across these 4 studies, the upper depression and anxiety prevalence recorded were high and ranged from 17% to 21%, respectively. The investigation conducted by Burnet et al., (2007) is one of the few studies to compare the rates of psychological distress in AS patients directly with those undergoing radical intervention. Burnet's findings reveal than men undergoing AS had over twice the prevalence of clinical anxiety as their counterparts being treated radically (21% and 10%, respectively). These findings clearly suggest that men being managed with AS are at a greater risk of developing psychological distress.

The clinical ramifications of unmanaged psychological distress in PCa patients being managed with AS is particularly large. A growing foundation of evidence suggests that for AS patients, anxiety acts as a significant independent predictor in determining which men will transfer to clinically unnecessary radical intervention in the absence of any meaningful disease progression (Latini et al., 2007; Patel et al., 2004).

In light of the increased utilisation of AS within the UK, it is imperative that health care professionals working with this patient group better understand the psychological impacts and

requirements of men undertaking this unique form of treatment so that more timely and effective frameworks for the identification and management of depression and anxiety can be put in place.

3.5.6. Direction of Future Research

A more definitive baseline estimate of depression and anxiety prevalence in a large cohort of AS patients is urgently needed. This would provide initial evidence from which to determine the degree and severity of psychological distress experienced by AS patients. This meta-analysis has revealed a clear shortfall of such research in the currently available literature.

The next stage in the programme of research being undertaken as part of the current PhD is to undertake a cross-sectional survey investigation into the prevalence of depression and anxiety in a large cohort of PCa patients being managed with AS. This will allow me to more accurately define the severity of the problem within this specific patient group. If such an investigation is to add meaningful and clinically relevant data to the current corpus of evidence, it will need to recruit a large sample of over 300 AS patients from multiple research centres within the UK. Such an approach will ensure that the results generated are more representative of, and thus generalisable to, the general population of AS patients within the UK.

It is hoped that such an investigation will provide a methodologically robust quantification of the likely prevalence of psychological distress experienced by AS patients. Such data will be of significant clinical importance in providing physicians and allied health care professionals working within this patient group with an increased awareness of the likelihood of psychological distress in the patients they treat. It is only once the awareness of such issues begins to grow that the clinical symptomology associated with depression and anxiety will be more readily identified by the clinical care team which will allow for the more effective and timely intervention and thus management of these debilitating psychological conditions.

3.5.7. Conclusion

The foundation of research relating to depression and anxiety prevalence among PCa patients is sizeable and growing steadily. However, much of the generated data are heterogeneous and had yet to be subjected to a rigorous systematic review and meta-analysis. This study has addressed this issue and provided the first systematic review and meta-analysis to date of depression and anxiety prevalence in PCa.

It was also a key aim of this study to determine how the prevalence of depression and anxiety vary across the trajectory of the treatment spectrum, from pre-treatment to post-treatment follow up. The results have highlighted that psychological morbidity in PCa patient varies widely over the trajectory of the disease. It appears that PCa patients experience the highest levels of depression and anxiety in the initial stages of diagnosis before any form of treatment has been initiated, before dropping off during the treatment stage and then rising again after the cessation of treatment.

Whilst this meta-analysis has shed some initial light onto the degree of psychological morbidity experienced by generic PCa patients over the course of the disease, the demographic and methodological heterogeneity observed within these studies means than only tentative conclusions can be made regarding these results.

This study has also revealed that only very limited and preliminary information regarding the prevalence of depression and anxiety among AS patients currently exists. It was an aim of this study to determine if any studies, other than those identified in the narrative literature review conducted in the previous chapter, measured depression and anxiety in AS patients. If they had it would have allowed me to extract these data to generate a more comprehensive estimate of prevalence rates specifically for AS patients. Unfortunately, no additional studies that recruited and measured depression and anxiety among a cohort of AS patients were identified.

Based on this shortfall of evidence it would appear important that future research aims to address this issue and focus on the assessment of depression and anxiety specifically among AS patients. As I develop the AS specific research program making up this PhD, the data I collect should significantly add to the foundation of research relating to the psychological well-being of PCa patients undergoing AS. This will positively impact on clinical practice for this cohort of elderly, chronically ill men who may be at a greater risk of psychological distress due to the unique nature of their treatment.

Chapter 4

A Cross-Sectional Assessment of Depression and Anxiety Prevalence in Prostate Cancer Patients Undergoing Active Surveillance

4.1. Research Question and Objectives

Research Question: What is the percentage prevalence of depression and anxiety in men with prostate cancer being managed with AS and are there any demographic variables that are associated with these conditions?

Research Objectives:

1. To define the percentage prevalence of clinically meaningful depression and anxiety in prostate cancer patients being managed with AS.
2. Conduct a large multicentre study with the capacity to;
    - Collect a variety of patient demographic data to allow me to determine if any of the major demographic variables were significantly associated with depression and anxiety.
    - Recruit AS patients from multiple NHS locations across the UK to enhance the generalisibility of the findings.
    - Open recruitment centres in geographical locations with a higher percentage of Afro-Caribbean men to maximise the chance of recruiting men of this ethnicity into the investigation.

4.2. Introduction

To the best of my knowledge, only four investigations have attempted to specifically recruit and assess depression and anxiety in PCa patients undergoing AS (Burnet et al., 2007; van den Bergh et al., 2009; van den Bergh et al., 2010; Steineck et al., 2002). Of these four investigations, only one has been conducted with British men (Burnet et al., 2007). Whilst the prevalence of depression and anxiety reported in this UK study was relatively low (12% and 21% respectively), the sample size was small (n=100) in comparison to those investigations which have assessed psychological distress in PCa patients undergoing radical treatment. The limited number of AS patients assessed for depression and anxiety currently makes it difficult to accurately define the likely prevalence of psychological morbidity within this patient cohort.

To ensure that depression and anxiety amongst AS patients is not both under-estimated and under-diagnosed, it is crucial that a more comprehensive and rigorous assessment of psychological distress be undertaken in this population. The primary aim of the current investigation was to address this issue by undertaking a large cross sectional assessment of the prevalence of clinically significant anxiety and depression in a large (300+) cohort of AS patients.

The previously conducted investigations into psychological distress in AS patients have recruited their samples exclusively from single centres. This has limited the generaliseabilty of their findings. Likewise, the previously conducted research has been plagued with high levels of homogeneity; over 92% of all AS patients assessed for depression and anxiety in the published literature have been of Caucasian ethnicity in comparison to less than 4% of men of Afro-Caribbean decent. Given the latter populations increased genetic predisposition to PCa (Ben-Shlomo et al., 2008), this represents a substantial void in our understanding of the psychological ramifications of AS in this ethnic group

Therefore it was also a key aim of the current investigation to ensure that I recruited AS patients from multiple centres across the United Kingdom to increase the diversity and generaliseabilty of the findings. Likewise, it was also a key aim to recruit a large proportion of AS patients of Afro-Caribbean descent to address the shortfall of research within this patient group.

It was hoped that doing so would provide a geographically diverse, ethnically varied, clinically relevant and more definitive estimate of the psychological health and well-being of this patient group for physicians and allied health care professionals working with the field of PCa. An improved research base within this area would facilitate health care teams working with AS patients, allowing for more efficient and effective assessment, identification and management of the psychological health and well-being of this unique patient group through their cancer journey.

4.3. Method

4.3.1. Study Design

The current investigation utilised a cross-sectional survey methodology. Before trying to understand the more complex patterns of depression and anxiety in AS patients, it was important to provide an initial estimate of how prevalent these conditions were in a UK population in the first place and how this might compare with the prevalence of anxiety and depression in the wider UK population of men this age without PCa.

A cross-sectional postal survey methodology was deemed the best methodological approach to do so for several reasons. Firstly, this approach has routinely been utilised among other cancer sites to provide an initial estimate of depression and anxiety prior to the running of more complex longitudinal investigations (Jadoon et al., 2010; Kissane et al., 1998;). Secondly, generating cross-sectional prevalence data in this way would create an appropriate scientific argument for more detailed and expensive studies that are able to tease out the details and correlations of these conditions.

A non-postal clinic based survey approach was also considered but was deemed impractical due to low clinic patient flow rates; AS patients typically only attend clinic once every 6-months. Recruiting my target sample size in this way would therefore take considerably longer than in a postal survey and would have been impossible to fund within a PhD. It was for this reason that a postal based cross-sectional survey was deemed the most appropriate methodology to adopt to allow me to reach my primary research objective of providing an initial baseline estimate of depression and anxiety prevalence that will underpin further more detailed study.

4.3.2. Survey Methodology

Once it was decided upon that a cross-sectional postal survey was the most appropriate methodology, it was important to develop a methodology that would maximise the validity and reliability of the results. This was done in the following ways:

VALIDITY

Within the research context, validity refers to the extent to which the investigation measures the variable(s) that it purports to be measuring. In the current investigation it was my specific aim to measure both depression and anxiety as unique and independent psychological

constructs. It was crucial to ensure that I developed a research protocol and utilised instruments that maximised the chances of doing so. The measures taken to address validity in the current investigation are described below.

- Instrument Validity

The primary research aim of the current investigation was to produce an estimate of depression and anxiety in a sample of AS patients. The most fundamental area of validity to address with regards to this aim was to ensure that I selected a questionnaire that was going to specifically and accurately identify and assess depression and anxiety. Failure to do so would undermine the validity of the generated findings. After careful consideration it was my decision to utilise the Hospital Anxiety and Depression Scale (HADS). My rationale for doing so and an overview and assessment of the validity and reliability of this instrument can be seen in 4.3.7 below.

- Sampling Bias

Sampling bias occurs within non-randomised investigations when participants self-select whether or not to take part in an investigation. An important risk associated with self-selected samples is that the final population recruited is not representative of the overall population due to a variety of confounders (overviewed in section 4.4). This was identified as a threat to population validity in the current investigation. To address this issue it was my initial aim to ensure that every AS patient at each recruiting hospital was contacted and invited to take part in the investigation. By utilising a "blanket" recruitment process such as this and targeting each AS patient at each of the 7 recruitment centres, I hope to minimise any sampling bias. Once recruitment had been finalised, it was my original aim to identify all non-responders and determine if they differed, clinically and demographically, from responders by their medical records.

Unfortunately, during the research ethics application process, Berkshire Research Ethics Committee (REC) strongly suggested that I anonymise the recruitment process to maximise data protection and remove the need for informed consent (see 4.3.3 below). I took the decision to follow Berkshire REC's advice and anonymise all questionnaire returns. Consequently it was not possible to identify non-responders as I had originally planned to determine if they differed to responders, either clinically or demographically. As a result I was not able to determine the representativeness of the recruited sample and this is an important

limitation driven by the requirements of the ethics committee which has impacted upon the population validity of the study.

However, the key aim of this study was to determine the prevalence of depression and anxiety in a large sample of AS patients. It has been well documented that depressed and anxious individuals are less likely to complete and return questionnaires in survey based research (Schofield et al., 2003). Therefore whilst I was unable to accurately determine the representativeness of the recruited population, it is likely that any data produced in regards to depression and anxiety prevalence would be an underestimation rather than an overestimation. To some extent this lessens the negative impact of my decision to anonymise recruitment at the expense of being able to account for sampling bias.

It was also important to note that the absence of any definitive normative data for depression and anxiety prevalence in AS patients meant that it was not possible to compare my sample with normative findings. The only comparably study was that conducted by Burnet and colleagues (2007). Whilst limited in scope, it was my intention to compare the findings generated from the current investigation with those produced by Burnet et al (2007).

- Sample Size

Unfortunately it was not possible to conduct a prospective power calculation to determine optimal sample size for this survey. This was because power calculations are only possible for hypothesis testing rather than estimation, as was the case in the current investigation.

Despite this it was important that I recruited a sample size that was large enough to provide reasonable precision in the prevalence estimation. The precision of an estimate is given by the size of the confidence interval associated with the estimate, usually set at 95%. The 95% confidence interval is given by + or – 2*sqrt(p(1-p)/n). As it is impossible to determine proportions (p) until after the study has been concluded it is necessary to use a likely estimate to enter into the equation. Based upon the advice of a statistician at the University of Southampton (Prof Philip Prescott), I set this at 15% (0.15). Using this value the confidence interval is generated using the 2*sqrt(0.15*0.85/n), which for n = 300 gives 2*sqrt(0.15*0.85/300) = 0.041. This corresponds to a value of 4%, suggesting that with a sample of 300 it would be possible to estimate the percentage of men who are depressed and anxious using a 95% confidence interval to within 4% of the true value. If I only recruited 100 men, this would increase to 7%. These initial calculations suggested that recruiting a sample of

300 AS patients would provide me with sufficient precision in the estimated prevalence data. It was for this reason that I set my recruitment target at 300.

RELIABILITY:

Reliability refers to the assumption that collected data would be the same in any given population over two or more time points. To maximise the reliability of the data collection process it was important to ensure that the questionnaire I utilised to measure depression and anxiety had good test-retest reliability. An overview and assessment of the reliability of the HADS can be seen in 4.3.7 below.

4.3.3. Research Ethics Committee

The current investigation received full ethical approval from the Berkshire Research Ethics Committee (REC Code 11/SC/0071; Appendix 8). During the REC meeting, which I attended in person, the Committee requested that I make several alterations to the original research proposal. The most significant of these involved my intended recruitment process. Originally it had been my aim to keep a record of each patient I contacted for entry into the current investigation. Patients would be required to complete and send back an informed consent form which would allow me to identify non-responders. All non-responders could then be re-contacted and if they decided not to take part I would have been able to determine if the non-responders differed from responders, either demographically or clinically, from their medical records (I was able to review patient records without consent as I was working in the PCa clinic as part of the patient's existing clinical care team under an Southampton University Hospitals Trust Honorary Contract). This would have helped me to determine the representativeness of my population.

However, the REC strongly suggested that I anonymise the recruitment process by removing the informed consent process and simply asking each patient to anonymously complete and return the questionnaires (see 4.3.6. recruitment procedures below). By anonymising the recruitment process, it was the REC's view that there would be less risk to patient confidentiality and less logistical demands upon the research team.

I subsequently decided to follow the REC's advice and anonymise the recruitment process in keeping with their recommendation. Whilst doing so simplified the recruitment process it prevented me from identifying non-responders. The associated risk of this was that firstly I was unable to follow up non-responders, which had a negative impact upon recruitment and

secondly I had no means of assessing the representativeness of the sample I eventually recruited.

4.3.4. Recruitment Sites

The lead site for the running, recruitment and sponsorship of this study was Southampton University Hospitals Trust. Six additional NHS Trust sites (Great Western NHS Trust, Mid-Essex NHS Trust Foundation, Coventry and Warwickshire NHS Foundation, Weston Area Trust Foundation, University College London Hospitals NHS Trust and Surrey and Sussex NHS Trust) were recruited as secondary sites to co-run the investigation in a bid to increase patient recruitment figures.

4.3.5. Participants

Participants for this investigation were recruited consecutively over a 7 month period from the prostate cancer clinic at Southampton General Hospital and the six additional NHS Trusts listed above. To be eligible for entry into the investigation, each participant had to meet each of the following criteria:

1. A biopsy confirmed diagnosis of PCa.
2. Diagnosis received at least two months prior to entry into the study to minimise acute, post-diagnosis mood disturbances.
3. Currently being managed with AS.
4. Be fluent in the English language (questionnaires were written and validated in English).
5. Have no additional cancer diagnoses.
6. Have no other serious or life threatening co-morbidity that could significantly impact upon mood.

4.3.6. Recruitment Procedures

The patient records at the prostate cancer clinic at Southampton General Hospital were screened to identify patients who were being managed with AS and met the inclusion criteria listed above. Once all eligible patients had been identified, they were sent a Patient Information Pack (PIP; Appendix 9). The PIP included a Patient Invitation Letter, a Hospital Anxiety and Depression Scale (Zigmond, & Snaith, 1983), a Patient Demographics questionnaire (see Instruments below) and a freepost return envelope addressed to the research team at Southampton University. As all patient questionnaire returns were to be anonymous, the need for informed consent, and the stringent data security measures that accompany personalised medical information, was not required

The Patient Invitation Letter (PIL) provided potential participants with an overview of the aims and purposes of the study along with instructions on what to do next should they wish to become involved in the study. If they wished to partake in the study, the PIL informed each participant to anonymously complete both of the enclosed questionnaires and send them back to the research team. Upon the receipt of the completed questionnaires the investigation recruitment procedures and the participant's involvement in the study were over.

4.3.7. Instruments Utilised

The Hospital Anxiety and Depression Scale

The primary aim of the current investigation was to provide an initial baseline estimate of the prevalence of depression and anxiety in a large sample of AS patients. Fundamental to this aim was the premise that I selected and utilised a questionnaire that would provide a valid and reliable assessment of depression and anxiety as specific psychological conditions. Failure to do so would have a substantial negative impact upon the generated findings. The following provides an assessment and overview of the validity and reliability of the HADS along with a rationale for my decision to utilise this questionnaire in the current investigation.

4.3.7.1. Overview of the HADS

The HADS is a two dimensional scale that was developed to identify depression and anxiety (Zigmond & Snaith, 1988). The HADS consists of 14 questions divided into two 7 question subscales:

1. Anxiety (HADS-A): 7 questions that assess generalised anxiety.
2. Depression (HADS-D): 7 questions that assess for general depression.

When completing the questionnaire, responders are asked to rate each of the 14 questions on a 4 point scale ranging from 0 (absence) to 3 (extreme presence). The total maximum score is 42 (21 on each of the two subscales, HADS-A and HADS-D). The scores are generated by summing the responses for each of the questions on both of the subscales. Higher scores indicate higher levels of depression and anxiety with a score of ≥8 on each of the subscales (HADS-D and HADS-A) representing the most commonly utilised score to identify caseness (see 4.3.7.5. below).

4.3.7.2. Validity of the HADS

- Bi-dimensionality

The HADS measures two independent psychological conditions; anxiety and depression. Fundamental to the validity of the HADS is the premise that it is able to distinguish between and measure anxiety and depression as independent and distinct conditions rather than as differing symptoms of general distress. Before finalising my decision to select the HADS it was important to ensure that it was able to discriminate between depression and anxiety.

A large number of investigations have assessed the independent bi-dimensionality (anxiety and depression) factor structure of the HADS using principle component analysis (Constantini et al., 1999; Dagnan et al., 2000; Lisspers et al., 1999; Moorey et al., 1991; Savard et al., 1998; Spinhoven et al., 1997). These investigations have supported the two-factor structure of the HADS in that all of the components identified fit into the dimensions of depression or anxiety. These findings suggest that the HADS is able to effectively distinguish between anxiety and depression dimensions.

Because the HADS should be able to effectively distinguish between depression and anxiety, correlation analyses between the HADS-A and HADS-D subscale should be weak; strong correlations would suggest a lack of distinctiveness. More than twenty independent investigations have assessed the factor structure and correlation between the HADS-A and HADS-D subscales and the results reveal a generally weak correlation (range: 0.40 – 0.56). Burns & Eidelson (1998) argue that for depression and anxiety on self-reported questionnaires to be considered strongly correlated, they should reach a 0.70 level. These findings suggest that the two subscales of the HADS are effective at measuring anxiety and depression as unique and independent conditions.

4.3.7.3. Internal Consistency

The internal consistency of the questions making up the two subscales of the HADS was an important issue to consider. Internal consistency relates to the ability of different questions within the same questionnaire to accurately and specifically measure the construct in question, in this case depression and anxiety. Low internal consistency would suggest that several questions exist within the HADS that fail to measure components of depression and anxiety. This would impact upon the validity of my findings.

Internal consistency is in most cases measured by Cronbach's alpha coefficient. Nunnally & Bernstein (1994) have argued that for a self-reported questionnaire to be deemed a valid measurement of a construct, the Cronbach's alpha coefficient should be at least 0.60, with a score of 1.00 being perfect and a score of 0.00 being non-existent internal consistency. More than 10 independent investigations have assessed the internal consistency of the HADS among patients with medical conditions (Constantini et al., 1999; Dagnan et al., 2000; Lisspers et al., 1999; Moorey et al., 1991; Savard et al., 1998; Spinhoven et al., 1998; Anderson, 1993; Bedford, Pau & Grant, 1997). Across these investigations, the Cronbach's alpha for the HAD-A ranged from 0.68-0.93 (mean 0.83) and for the HADS-D from 0.67-0.90 (mean 0.82). These findings would suggest that that the HADS is a robust instrument for the measurement of depression and anxiety.

4.3.7.4. Concurrent Validity

The third important issue to address regarding the validity of the HADS was to ensure that it had a high level of concurrent validity. Concurrent validity refers the ability of a questionnaire to generate results that positively correlate to those produced by an established questionnaire that has been previously validated. Relating specifically to the assessment of depression and anxiety, such validation is usually against a structured clinical interview or clinician diagnosis. If positive correlations are observed, it suggests that the questionnaire in question is effective at measuring what it purports to be measuring.

Over 20 independent investigations have assessed the validity of the HADS against established measures of depression and anxiety (Lisspers et al., 1999; Watson et al., 1995; Savard et al., 1998). These included the Structured Clinical Interview (utilising the DSM-III and IV criteria), the Beck Depression Inventory, the General Health Questionnaire, the State-Trait Anxiety Inventory, the Montgomery-Asberg Depression Rating Scale, the Clinical Anxiety Scale, the Hamilton Anxiety Scale and the Hamilton Rating Scale for Depression. Across all of these concurrent validity assessments, correlations ranged from 0.60-0.86 (mean 0.75). These findings would suggest that the HADS has a high level of validity in assessing depression and anxiety.

4.3.7.5. Caseness cut-off scores

In their original article, Zigmond & Snaith (1983) recommended a cut-off score of 8 to identify patients with mild but clinically meaningful levels of depression and anxiety. Since then dozens of independent investigations have assessed the sensitivity of varying cut-off scores on the

HADS to determine depression and anxiety to assess whether the utilisation of a higher or lower cut-off score would increase the sensitivity of the instrument (Lam et al., 1995; Hall et al., 1999; Ravazi et al., 1990). Across these investigations, optimal sensitivity was obtained when a cut-off scores of 8 was utilised as assessed against structured or semi-structured clinical interviews utilising the DSM criteria. As a result of the weight of evidence generated by these investigations, I decided to utilise a cut-off score of 8 in the current investigation to identify men with meaningful depression and anxiety. An additional benefit of doing so was that in the only other UK based investigation into depression and anxiety in AS patients, Burnet and colleagues also utilised a cut-off score of 8 on the HADS (Burnet et al., 2007). This would allow for a direct comparison between the results produced by my investigation and those published by Burnet.

4.3.7.6. Reliability of the HADS

For the results of the current investigation to be meaningful, it was crucial that I utilised a questionnaire the generated reliable measures of depression and anxiety. Assessing test-retest score variations is an acceptable approach to determine instrument reliability (Herrmann, 1997). Test-retest reliability refers to the ability of any given questionnaire to produce similar results when completed by the same individual/population on two time points. If an instrument produces similar scores across time points then the reliability of that instrument can be deemed to be good, based upon Pearson correlation coefficient scores (0=non-existent correlation; 1=perfect correlation).

In a large meta-analysis, Hermann (1997) revealed that the test-retest reliability of the HADS was excellent when the test were re-administered within two weeks of each other (r=0.84-0.85) and adequate to excellent when re-administered 2-6 weeks of each other (r=0.73-0.76). These results suggest that the HADS is a reliable instrument for the assessment of depression and anxiety.

4.3.7.7. Possible alternatives

Depression and anxiety are extremely common psychological conditions and as such there are many and varied questionnaires available for their assessment. Some of the most commonly utilised include the Beck Depression Inventory, the State-Trait Anxiety Inventory, the Montgomery-Asberg Depression Rating Scale, the Clinical Anxiety Scale, the Hamilton Anxiety Scale and the Hamilton Rating Scale for Depression. All of these instruments have been

extensively assessed and offer a valid and reliable assessment of depression and anxiety. Despite this, it way my decision to ultimately select the HADS based upon two key reasons.

Firstly, many of the questionnaires available for the assessment of depression and anxiety do so individually. For example, the Beck Depression Inventory measures only depression whilst the State-Trait Anxiety Inventory measures only anxiety. Whilst both of these questionnaires offer excellent reliability and validity, their use would have entailed utilising two individual questionnaires. This would have placed additional time demands upon the patients I hoped to contact. It was an express wish of the Berkshire REC that I minimise the number of questionnaires I planned to send to my target population. By choosing to use the HADS, I was able to produce valid and reliable results from one single questionnaire. This appeared to be a key advantage of the HADS over possible alternatives such as those listed previously.

Secondly, the only other investigation into the assessment of depression and anxiety in AS patients within the UK utilised the HADS as their measure of depression and anxiety. Given the paucity of research within this area, and the absence of any other normative data with which to compare my findings, utilising the HADS would allow me to directly compare my findings with those generated by Burnet et al (2007). This is particularly true given that Burnet also utilised a HADS cut-off score of 8.

Therefore whilst other instruments for the measurement of depression and anxiety were considered, I ultimately decided upon the HADS. This was due to the good validity and reliability it offered, the fact that it assessed both depression and anxiety in one concise questionnaire and would produce results that were directly comparable to those reported by Burnet et al (2007). A copy of the HADS can be seen in Appendix 9.

The Patient Demographic Questionnaire (PDQ) :

The Patient Demographic Questionnaire (PDQ) was developed by the research team at the University of Southampton to measure the key demographic information required for this study and included information on participant age, ethnic status, employment status, relationship status and educational status. These data would allow me to determine whether any of the recorded demographic variables were significantly associated with depression and anxiety which was one of my key research aims. A copy of the PDQ can be seen in Appendix 9.

4.3.8. Data Collection and Analysis

As each completed HADS and PDQ was received, the data from both questionnaires were entered into a predetermined Excel spread sheet. This data was then transferred to SPPS 19.0 for analysis.

The primary aim of the current investigation was to define the prevalence of clinically meaningful depression and anxiety in a large sample of AS patients. The outcome for this aim was the percentage prevalence of depression and anxiety. To quantify this research aim descriptive statistics were computed to estimate the percentage prevalence of depression and anxiety (i.e. the % scoring ≥8 on each HADS subscale).

A secondary aim of the current investigation was to determine if any of the demographic variables were significantly associated with depression and anxiety. To determine this, each of the collected demographic variables (age, employment, ethnicity, education and NHS Trust location) were cross tabulated against patients who were identified as depressed or anxious to allow me to identify if any of these variables were significantly associated with a higher prevalence of depression and/or anxiety. The chi-squared test was used to assess for significance at the 0.05 level. Logits transformations to the proportions was applied (performed automatically by SPSS) to guard against non-normality.

Finally, in order to determine predictors for depression and anxiety, multiple linear regressions were conducted, with $p<0.05$ considered as statistically significant.

4.4. Results

4.4.1. Patient Demographics

313 participants out of an approached sample of 420 (response rate: 74.52%) were recruited from seven NHS Trust sites into the current investigation. Table 7 below summarises the demographic characteristics of the study sample.

Table 7: Patient Demographic Characteristics

Site	S'ton	Swindon	Essex	Coventry	Weston-S-Mare	UCLH	Sussex & Surrey	All
Number of responders:	*28/36*	89/113	14/18	92/121	15/24	23/37	52/71	313
Age (years):								
Mean (SD)	*73.0 (8.598)*	71.9 (7.276)	66.5 (2.953)	67.93 (5.441)	77.93 (5.849)	68.13 (5.684)	68.08 (5.577)	70.49 (7.335)
Range	*55-90*	53-72	62-72	50-79	71-81	51-77	50-81	51-90
Employment Status:								
Full-time employment	4	10	0	16	0	7	4	41
Part-time employment	4	5	4	3	0	6	6	28
Retired	19	72	7	69	15	10	42	234
Unemployed	1	1	0	3	0	0	0	5
Unknown	*0*	1	3	1	0	0	0	5
Relationship Status								
Co-habiting	2	5	0	1	0	2	4	14
Divorced	4	0	1	5	2	2	2	16
Married/civil partnership	18	70	10	75	9	17	40	239
Single	0	2	0	7	0	2	5	16
Widowed	4	11	0	3	4	0	1	23
Unknown	0	1	3	1	0	0	0	5
Education status								
Left school before age 15	3	23	0	18	4	0	8	56
Completed secondary education	18	27	6	27	6	5	17	106
College/specialised training	5	31	3	34	4	5	17	99
University	2	7	2	12	1	13	10	47
Unknown	0	1	3	1	0	0	0	5
Ethnicity								
White British	28	85	11	87	15	19	51	296
White Other	0	1	0	3	0	2	0	6
Afro-Caribbean	0	2	0	0	0	2	0	4
Asian	0	0	0	2	0	0	1	3
Other	0	1	0	0	0	0	0	1
Unknown	0	0	3	0	0	0	0	3

The mean age of the patients was 70.49 years (range, 51-90). Most participants were retired and (74.44%) married/in civil partnership (76.99%). 36.6% completed their education to secondary school level, whilst 32.3% completed college/specialised training. The large majority

of participants (93.8%) were of British White ethnicity. 8 men did not disclose their age, and 5 did not complete the remainder of the demographic questions.

4.4.2. Prevalence of Depression and Anxiety

Depression: Across the 313 participants, mean depression was 3.269 (SD=3.569), with scores ranging from 0 to 18. 12.46% (n=39) of participants obtained a score of ≥8 on the HADS-D, indicating the existence of clinically meaningful levels of depression (Table 8).

Anxiety: Across the 313 participants, mean anxiety was 4.84 (SD=3.791), with scores ranging from 0 to 20. 23.32% (n=73) of participants obtained a score of ≥8 on the HADS-A, indicating the existence of clinically meaningful levels of anxiety (Table 8).

Table 8: Mean HADS scores

	Mean (with 95% CIs	**Standard Error**	**Median**	**Standard Deviation**	**Min**	**Max**	**Caseness (HADS≥8)**
HADS – D (Depression)	3.269 (2.9-4.3)	0.281	2	3.569	0	18	N=39 (12.46%)
HADS – A (Anxiety)	4.84 (4.4-5.3)	0.299	4	3.791	0	20	N= 73 (23.32)

4.4.3. Cross tabulations

Each of the collected demographic variables (age, employment, relationship, ethnicity, education and NHS Trust location) were cross tabulated against patients who were depressed and/or anxious to allow me to identify if any of these variables were associated with a higher prevalence of depression and anxiety.

Cross tabulations for depressed patients

Eight participants did not record their age in their completed questionnaire responses. These participants were excluded from all analyses that included age as a predictor variable.

Depression and Age: The mean ages for the depressed and non-depressed participants were not significantly different at 69.8 and 70.3 years, respectively, suggesting age was not associated with a higher prevalence of depression (Table 9).

Table 9. Depression and Age Cross Tabulation

	N	Mean	Std. Deviation	Std. Error Mean
Non Depressed	274	70.30	6.87	0.42
Depressed	31	69.80	7.90	1.31

Depression and Employment: Most participants were retired or in full or part time employment with the percentages of depressed men ranging from 11.1% to 25%. No significant differences were observed in the depression scores across the five employment categories (Table 10)

Table 10: Depression and Employment Cross Tabulation

	Full Time	Part Time	Retired	Unemployed	Total
Non Depressed (n)	36	23	208	4	271
% Within Employment	87.8%	82.1%	88.9%	75%	88%
Depressed (n)	5	5	26	1	37
% Within Employment	12.2%	17.9%	11.1%	25%	12%
Total	41	28	234	5	308

Chi-square = 1.861, P=0.628

Depression and Relationship: The majority of participants (n=239) were married and living with their partner. Those who were single (n=16) had the highest percentage of depressed men (25%). However, the differences in the percentages of depressed participants across the five relationship categories was not significant (Table 11).

Table 11: Depression and Relationship Cross Tabulation

	Co-Habiting	Divorced	Married	Single	Widowed	Total
Non Depressed (n)	12	14	211	12	22	271
% Within Relationship	85.7%	87.5%	88.3%	75%	95.7%	88%
Depressed (n)	2	2	28	4	1	37
% Within Relationship	14.3%	12.5%	11.7%	25%	4.3%	12%
Total	14	16	239	16	23	308

Chi-square = 3.924, P=0.410

Depression and Ethnicity: 95.79% of participants (n=296) were of the same ethnic group (White British). Due to this homogeneity, no meaningful results were produced from this cross tabulation (Table 12). As a result of this, ethnicity was subsequently removed as a variable from all further analyses.

Table 12: Depression and Ethnicity Cross Tabulation

	Asian	Afro-Caribbean	Other	White British	White Other	Total
Non Depressed (n)	3	4	1	260	5	273
% Within Ethnicity	100%	100%	100%	87.8%	83.3%	88%
Depressed (n)	0	0	0	36	1	37
% Within Ethnicity	0%	0%	0%	12.2%	16.7%	12%
Total	3	4	1	296	6	310

Chi-square = 1.087, P=1.000

Depression and Education: Depression prevalence was slightly higher in participants who left school before the age of 15 or completed secondary education in comparison to those who went on to college/specialist training or university. However, this difference was not significant (Table 13).

Table 13: Depression and Education Cross Tabulation

	College/Specialist	Left School <15	Secondary Education	University	Total
Non Depressed (n)	89	46	93	43	271
% Within Education	89.7%	82.1%	87.7%	91.3%	88%
Depressed (n)	10	10	13	4	37
% Within Education	10.3%	17.9%	12.3%	8.7%	12%
Total	99	56	106	47	308

Chi-square = 1508, P=0.833

Depression and NHS Trust site: The only significant differences in percentages of depressed men occurred in the site groupings with higher percentages in Southampton (35.7%) and Essex (21.4%) (Table 14).

Table 14. Depression and NHS Trust Site Cross Tabulation

	Coventry	Essex	UCLH	Sussex & Surrey	Soton	Swindon	Weston-S-Mare	Total
Non Depressed (n)	84	11	21	48	18	77	15	274
% Within Site	91.3%	78.6%	91.3%	92.3%	64.3%	86.5%	100%	87.5%
Depressed (n)	8	3	2	4	10	12	0	39
% Within Site	8.7%	21.4%	8.7%	7.7%	35.7%	13.5%	0%	12.5%
Total	92	14	23	52	28	89	15	313

Chi-square = 19.712, P=0.004

Cross tabulations for anxiety

As for the depression cross tabulations above, eight participants did not record their age in their completed questionnaire responses. These participants were excluded from all analyses that included age as a predictor variable.

Anxiety and Age: The mean ages for the anxious and non-anxious participants were not significantly different at 68.9 and 70.7 years, respectively, (Table 15).

Table 15: Anxiety and Age Cross Tabulation

	N	Mean	Std. Deviation	Std. Error Mean
Non Anxious	236	70.66	7.00	0.45
Anxious	69	69.91	6.82	0.81

Anxiety and Employment: The percentages of anxious men ranged from 20.9% to 60%. No significant differences were observed in the percentages of anxious men across the five employment categories (Table 16).

Table 16: Anxiety and Employment Cross Tabulation

	Full Time	Part Time	Retired	Unemployed	Total
Non Depressed (n)	29	21	185	2	237
% Within Employment	70.7%	75%	79.1%	40%	76.9%
Depressed (n)	12	7	49	3	71
% Within Employment	29.4%	25%	20.9%	60%	23.1%
Total	41	28	234	5	308

Chi-square = 6.517, P=0.161

Anxiety and Relationship: There was a significantly higher percentage of anxious participants in the divorced category (56.3%) than in the married, co-habiting, single or widowed categories (Table 17)

Table 17: Anxiety and Relationship Cross Tabulation

	Co-Habiting	Divorced	Married	Single	Widowed	Total
Non Anxious (n)	10	7	187	12	21	237
% Within Relationship	71.4%	43.8%	78.2%	75%	91.3%	76.9%
Anxious (n)	4	9	52	4	2	71
% Within Relationship	28.6%	56.3%	21.8%	25%	8.7%	23.1%
Total	14	16	239	16	23	308

Chi-square = 13.114, P=0.011

Anxiety and Ethnicity: 95.79% of participants (n=296) were of the same ethnic group (White British). Due to this homogeneity, no meaningful results were produced from this cross tabulation (Table 18). As a result of this, ethnicity was subsequently removed as a variable from all further analyses.

Table 18: Anxiety and Ethnicity Cross Tabulation

	Asian	Afro-Cari	Other	White British	White Other	Total
Non Anxious (n)	3	4	1	226	5	239
% Within Ethnicity	100%	100%	100%	76.4%	83.3%	77.1%
Anxious (n)	0	0	0	70	1	71
% Within Ethnicity	0%	0%	0%	23.6%	16.7%	22.9%
Total	3	4	1	296	6	310

Chi-square = 5.506, P=0.356

Anxiety and Education: There were no significant differences in the percentages of anxious men across all four education categories (Table 19).

Table 19: Anxiety and Education Cross Tabulation

	College/Specialist	Left School <15	Secondary Education	University	Total
Non Anxious (n)	79	39	83	36	237
% Within Education	79.8%	69.6%	78.3%	76.6%	76.9
Anxious (n)	20	17	23	11	71
% Within Education	20.2%	30.4%	21.7	23.4	23.1%
Total	99	56	106	47	308

Chi-square = 0.550, P=0.964

Anxiety and NHS Trust Site: There were no significant differences in percentages of anxious men in the site categories but a higher percentage of anxious men was observed in Essex (42.9%) and Southampton (32.1%) (Table 20).

Table 20: Anxiety and NHS Trust Site Cross Tabulation

	Coventry	Essex	UCLH	Sussex & Surrey	Soton	Swindon	Weston-S-Mare	Total
Non-Anxious (n)	73	8	16	43	19	69	12	240
% Within Site	79.3%	57.1%	69.6%	82.7%	67.9%	77.5%	80%	76.7%
Anxious (n)	19	6	7	9	9	20	3	73
% Within Site	20.7%	42.9%	30.4%	17.3%	32.1%	22.5%	20%	23.3%
Total	92	14	23	52	28	89	15	313

Chi-square = 6.403, P=0.383

4.4.4. Prediction of Depression and Anxiety using Demographic Variables

Since the demographic variables Employment, Relationship, Education and Site were categorical variables, separate indicator variables were created for the various categories such as Full-time, Part-time, Divorced, Married, etc. Reference categories were then selected for each of the four categorical variables as follows:

Employment: Full-time.
Relationship: Married,
Education: University,
Site: London.

Any coefficients for variables included in the fitted models are relative to the reference categories. A score of ≥8 on the HADS questionnaire was utilised in the current investigation as being indicative of clinically meaningful depression and anxiety. Logistic regression analysis was used to investigate whether any of the demographic variables had significant predictive value in identifying depressed and anxious participants who scored ≥8 on the HADS.

4.4.4.1. Predictions of Depression

When Age was included as a possible predictor, 8 men were removed from the analyses because of missing age data. Since Age was not found to be a predictor, the analyses were repeated without Age so that all 313 men could be included. The results are given below (Table 21).

Table 21: Correct classifications declaring all participants as non-depressed

Non-depressed	274	100%
Depressed	39	0%
Overall Percentage	0	87.50%

Table 21 shows that without any predictor variables, the percentage of correct classifications is 87.5% obtained by declaring all men to be not depressed. The objective of the logistic regression model was to determine if any of the demographic variables acted as significant predictors to increase this percentage of correct allocations.

Each demographic variable used as a possible predictor was assessed to determine whether it could be included in the model to improve its predictive value. A stepwise analysis was utilised for this purpose, entering or removing variables at each step where the p-value for entry was taken by default as 0.05. If any variable entered into the model at an earlier step becomes insignificant at a later step, it was removed from the model using the default values selected by SPSS. The results of this stepwise analysis indicated that Southampton was the 'best' single predictor with a p-value < 0.0005. None of the other variables were significant with the next lowest p-value being 0.119 for Single, (table 22).

Table 22: Significant predictors of depression

Full time	0.003	1	0.956

Part time	0.821	1	0.365
Retired	1.547	1	0.214
Semi-retired	0.143	1	0.706
Unemployed	0.584	1	0.445
Co-habiting	0.045	1	0.832
Divorced	0	1	0.996
Married	0.514	1	0.473
Single	**2.431**	**1**	**0.119**
Widowed	1.498	1	0.221
Asian	0.287	1	0.594
BA	0.143	1	0.706
BC	0.431	1	0.511
Chinese	0.143	1	0.706
WB	0.443	1	0.505
WO	0.099	1	0.753
College	0.265	1	0.607
Specialist College	0.596	1	0.44
Left School <15	0.129	1	0.719
Secondary	0.215	1	0.643
University	0.701	1	0.403
Coventry	1.693	1	0.193
Essex	1.081	1	0.299
London	0.323	1	0.57
SASH	1.3	1	0.254
Southampton	**15.245**	**1**	**0**
Swindon	0.119	1	0.73
Western-S-M	2.243	1	0.134

Table 23 shows the estimated model parameters at Step 1 of the logistic regression with only Southampton included, and also shows that at Step 2, with Southampton already in the model, the variable Single is entered as the next most significant predictor with a p-value of 0.055 which is almost significant. The odds ratio for Southampton was 4.904 and 5.422 for both steps 1 and 2, indicating that there is a higher chance of being depressed amongst the men from Southampton.

Table 23: Logisitic regression for depression with 95% confidence intervals

		B	S.E.	Wald	df	Sig	Odds Ratios	95% CIs
Step 1:	Southampton	1.590	.440	13.037	1	.000	4.904	2.07-11.62
	Constant	-2.178	.196	123.555	1	.000	.113	
Step 2	Single	1.180	.614	3.687	1	.055	3.253	0.97-10.84
	Southampton	1.691	.447	14.314	1	.000	5.422	2.26-13.02
	Constant	-2.278	.210	117.705	1	.000	.102	

In Table 23 we see that the Wald statistic, which tests whether each term is required in the model, indicates that at both steps 1 and 2 Southampton is significant with a p value < 0.0005, which is highly significant, but that at step 2 Single is not quite significant with a Wald statistic p-value of 0.055.

However when these variables were included in the logistic regression model in turn and the probability of being a depressed man was evaluated for each subject (Table 24 below) none of the probabilities were increased sufficiently to change the proportion of correctly classified men. The cut-off value for the estimated probability of being depressed was taken to be 0.5. Referring back to Table 21 above, we can see that without any of the demographic variables included, the model is able to correctly predict 87.5% of depressed men, meaning the addition of "Southampton" and "Single" into the model produced no additional predictive value.

Table 24: Classification of depressed men with the inclusion of Southampton and Single

Soton	Non-depressed (n=274)	100%
	Depressed (n=39)	0%
	Overall % Classification	**87.50%**
Soton & Single	Non-depressed (n=274)	100%
	Depressed (n=39)	0%
	Overall % Classification	**87.50%**

4.4.4.2. Predictors of Anxiety

The logistic regression analysis performed for depression was repeated to investigate predictions of anxiety using the demographic variables. As with depression, Age was removed once it was confirmed to be insignificant in order to use all 313 men in these analyses. Table 24 below shows that 76.7 % of correct predictions would be produced by declaring all men not to be anxious using no predictor variables in the model.

Table 24: Correct classifications declaring all participants as non-anxious

	Observed	Percentage Correct
Non-Anxious	240	100%
Anxious	73	0%
Overall Percentage	0	76.7%

Each variable used as a possible predictor was assessed to see whether it could be included in the model to improve its predictive value. Table 25 below indicates that "divorced" was the most significant predictor.

Table 25: Significant predictors of anxiety

Full time	0.993	1	0.334
Part time	0.048	1	0.826
Retired	2.943	1	0.086
Semi-retired	3.298	1	0.069
Unemployed	1.612	1	0.204
Co-habiting	0.226	1	0.635
Divorced	**10.223**	**1**	**0.001**
Married	1.385	1	0.239
Single	0.027	1	0.871
Widowed	2.97	1	0.085
Asian	0.612	1	0.434
BA	3.298	1	0.069
BC	0.921	1	0.337
Chinese	0.305	1	0.581
WB	0.373	1	0.542
WO	0.343	1	0.558
College	0.031	1	0.859
Specialist College	0.158	1	0.691
Left School <15	0.058	1	0.809
Secondary	0.009	1	0.923
University	0.426	1	0.514
Coventry	0.52	1	0.471
Essex	3.127	1	0.077
London	0.702	1	0.402

SASH	1.262	1	0.261
Southampton	1.338	1	0.247
Swindon	0.05	1	0.822
Western-S-M	0.097	1	0.755

None of the other variables were significant so only Divorced was included in the logistic model. The logistic regression parameter estimates for predicting Anxiety using divorced are shown in Table 27.

Table 27: Logistic regression analysis for anxiety with 95% confidence intervals

		B	S.E.	Wald	df	Sig	Odds Ratios	95% CIs
Step 1:	Divorced	1.543	.523	8.698	1	0.003	4.681	1.681-13.055
	Constant	-1.292	.141	83.832	1	.000	0.275	

Table 27 shows the odds ratio for Divorced is 4.68 with confidence interval 1.68 to 13.05. This is significant with p = 0.003, indicating that divorced men are more likely to be anxious. Including this term in the model increases the estimated probability of being anxious for the divorced men sufficeently for there to be a small increase in the proportion of correctly identified anxious men, see Table 28 below. This small increase from 76.7% to 77.3%, although significant, does not have any clinical relevance.

Table 28: Classification of anxious men with the inclusion of Divorced

Level	Observed	Percentage Correct
Divorced	Non-anxious (n=233)	97%
	Anxious (n=64)	12%
	Overall % Classification	**77.30%**

4.5. Discussion

Over the last decade there has been a well-documented increase in the utilisation of AS for the management of localised PCa. The benefits of such an approach are clear; patients placed onto an AS protocol avoid the risks of surgical intervention, which can include infections, septicaemia and in rare instances death (Kirby & Tailor, 2008). Surgical intervention is also associated with diminished quality of life and chronic and debilitating urinary and sexual

dysfunction (Vesey et al., 2012). It is vital to understand and to convey to AS patients that those managed with observation do not experience any significant reductions in 12 year survival through opting for non-invasive treatment (Wilt et al., 2012).

Despite these clear benefits, AS is not without associated side effects. From a physical perspective, urinary problems are commonplace. However, perhaps the biggest unanswered question concerning the negative sequelae of AS relates to psychological morbidity. Very little is currently known or understood about the negative psychological side effects of being managed with AS and living for prolonged periods of time with an "untreated" cancer.

Very few studies have attempted to define this issue. The aim of the current investigation was to address this issue and conduct a large, definitive and multi-centred cross-sectional survey into the prevalence of clinical depression and anxiety in PCa patients being managed with AS.

4.5.1. Key Findings

Depression Prevalence

Across the 313 AS patients recruited into the current investigation, the mean group prevalence of clinical depression was low at 3.27 (SD 3.33). However, using the standardised threshold of 8 or above on the HADS (Zigmond & Snaith., 1983) to define depression in any individual, 12.46% (n=39) of participants met the criteria for clinically significant depression. A large normative assessment of depression in the general population of UK adults utilising the HADS (n=1792) revealed that mild-moderate depression (≥8) was observed in 7.8% of participants (Crawford et al., 2001).

Anxiety Prevalence

Across the 313 AS patients, the mean group prevalence of clinical anxiety was again relatively low at 4.84 (SD 3.85). However, the prevalence of clinical anxiety was high at 23.32% (n=73) based upon the standardised threshold of 8 or above on the HADS which defines anxiety for any individual. As was observed for depression, the large normative assessment of anxiety in the general population of UK adults (utilising the HADS; n=1792) revealed that mild-moderate anxiety (≥8) was observed in 20.6% of participants.

Demographic Variables

A variety of demographic variables were collected in the current investigation. This was done to determine if any of the variables were associated with depression and anxiety prevalence. The implications and interpretation of these data will be considered later in the discussion.

4.5.2. Strengths and Weaknesses

Whilst the findings provide the largest and most definitive estimate of the prevalence of clinical depression and anxiety in AS patients to date, important limitations exist which must be considered when interpreting these findings.

Firstly, the current study utilised a cross-sectional design. Such an approach was unable to take into account changes in anxiety and depression over time. It is well documented that anxiety peaks among PCa patients in the three to four week prior to PSA testing and subsides substantially if the subsequent clinical outcome indicates a lack of disease progression (Lofters et al., 2002). Likewise, the prevalence of psychological distress in AS patients is generally highest in the 12-15 months post diagnosis and then subsides (Davidson et al., 2009). This may be due to patients developing an increased acceptance of AS and the idea of living with an "untreated" cancer. It is also likely that the absence of any meaningful disease progression in the first 15-months post-diagnosis reassures the patient that their disease is stable and future progression is unlikely.

The cross-sectional nature of the current investigation, coupled with the anonymous recruitment process adopted, meant that it was not possible to account for such changes over time nor determine where each patients was in regards to both their PSA monitoring schedule and how long ago they were diagnosed. Both of these issues would likely have had a large impact upon the depression and anxiety scores recorded.

During the recruitment phase of the current investigation I identified this problem and took measures to address it. I applied for a Substantial Amendment to the Berkshire Research Ethics Committee (REC) that would allow me to ask each patient to record their date of diagnosis on the Patient Demographics Questionnaire. This would allow me to determine if any positive correlations existed between the prevalence of depression and anxiety observed and time since diagnosis.

This Substantial Amendment was approved by the Berkshire REC in November 2012 and all patients subsequently recruited into the study were asked to record their date of diagnosis. Unfortunately, this was in the latter stages of recruitment and only 56 patients were recruited

during this period. Of these 56 patients, only 16 recorded their date of diagnosis on the questionnaires they returned. Such small numbers precluded any meaningful statistical analysis on these data. If these data had have been recorded from the start of recruitment, it would have provided an important insight into how the trajectory of psychological distress alters in the months and years after initial diagnosis. This represents an important limitation and it is important that future research addresses this issue.

Secondly, a key exclusion criteria of this investigation was that AS patients with serious co-morbidity were to be excluded from entry into the study. This was an important criteria as the aim of this study was to determine the level of psychological distress in men on AS. If AS patients with advanced chronic kidney disease, debilitating heart disease or Parkinson's disease were recruited, it is probable that these conditions would substantially impact upon mood, possibly more so than their localised and potentially asymptomatic PCa.

However, the application of this exclusion criteria was challenging and created several limitations that need to be considered. Firstly, in order to apply the criteria, it was firstly necessary to define "other serious co-morbidity". It was impractical to list every type of morbidity this could include but a variety of illnesses were covered and listed based upon the advice of two clinicians which included, for example, late stage kidney disease, advanced cardiovascular disease and stroke.

When each new recruitment site was confirmed, I had an in-depth tele-conference with the research nurses who would be running the project. During this meeting all of the issues relating to recruitment standardisation and the application of the inclusion and exclusion criteria were discussed and clarified. It was confirmed and reiterated with all of the research nurses that should they find a patient with borderline co-morbidity that they were unsure as to whether or not to include or exclude, the nurses were to contact me for clarification, which was decided upon in conjunction with my supervisors.

However, the inherently subjective nature identifying and defining "other serious co-morbidity" meant that much variation across the research sites could have occurred. Consequently, some men may have been included at one site that would have been excluded at another, depending upon the interpretation and application of this criteria by the clinical care team running the recruitment.

Likewise, the failure to ask each of the research sites to log the number of AS patients eligible for inclusion who were not approached due to having serious co-morbidity meant that I was

unable to quantify the impact of this limitation. This represents an important limitation to the study but one that was driven by logistical necessity; each of the research nurses running the recruitment of this study at their respective sites were extremely busy and in many cases under-staffed. A key reason that they agree to participate was that it was an easy and undemanding study to co-run. I felt that if I had asked them to log and manage factors such as the number of patients identified who were not approached due to co-morbidity then it may have jeopardised their willingness to partake.

Thirdly, a variety of confounders exist which cannot be explained by the methodology I adopted. For example, depressed and anxious patients are less likely to complete and return questionnaires than their non-depressed and non-anxious counterparts (Schofield et al., 2003). It is therefore likely that the anxiety and depression prevalence data generated through the current investigation was an underestimation; those who responded may have had a far lower level of depression and anxiety than those who failed to respond. This means that the results generated may not be representative of generic AS patients within the UK. Such an issue does not lessen the implications of these findings as it suggests that the high prevalence data observed is an underestimation of that which is likely to exist in the general UK population of AS patients. Given that the overriding aim of this PhD was to allow for the better understanding and management of depression and anxiety within the AS population, the fact that the prevalence of these conditions is likely to be higher than currently estimated adds additional support for, rather than detracting from, the need for a framework to allow for the better management of these conditions.

Another potential confounder that may have had an impact upon the depression and anxiety prevalence data generated was that of urinary incontinence. Urinary incontinence is common among men living with PCa and is estimated to effect over 80% of patients (Walsh et al., 2000). Incontinence is substantially higher in men who have undergone radical intervention in comparison to those being managed with AS yet estimates suggest that between 10%-20% of AS patients still experience a degree of incontinence (Soloway et al., 2010). Evidence exists to support a causal link between urinary dysfunction and psychological distress in PCa patients (Balderson & Towel, 2003; Hara et al., 2003). It is possible that urinary incontinence may have been an important predictive factor in determining which of the AS patients recruited into the current investigation were depressed or anxious. The failure to account for and assess urinary incontinence rates is a key limitation of the findings of the current investigation. Had such information been collected, it would have been possible to determine whether rates of

incontinence predicted which men were most likely to be experiencing depression and anxiety. If such a relationship was found to exist, it would provide a novel area for future research to address to help AS patients better cope and manage with issues relating to incontinence as a means of lowering depression and anxiety. Additional research into this area would be beneficial.

Fourthly, there exist a variety of factors that could have been built into the methodology to improve the design of the study. Firstly, my decision to utilise the HADS as the primary measure of depression and anxiety was driven by the validity and reliability if offered and the fact that it would allow direct comparison with the other AS specific research which has also utilised the HADS. However, as a generic measure of depression and anxiety, it has little specific relevant to PCa. To address this it would have been extremely beneficial to include a PCa specific measure of distress, such as the Memorial Anxiety Scale for Prostate Cancer (MAX-PC). This would have allowed me to assess how and in what ways PCa was specifically impacting upon the prevalence of distress observed.

Secondly, my decision to adopt the anonymous recruitment policy recommended by the ethics committee was a key one as it prevented me from being able to compare responders with non-responders, both clinically and demographically. However, it would have been possible to have applied for a Substantial Amendment to allow me to adopt my initial non-anonymous recruitment protocol (asking for signed informed consent from each patient) at one or two local sites, such as Southampton and Swindon. Doing so would have allowed for a sub-group analysis between responders and non-responders. Whilst such findings could not be generalised to the other sites, it would have provided an important and interesting insight into the clinical and demographic differences between responders and non-responders.

Thirdly, this study did not recruit a cohort of PCa patients who were receiving radical treatment. I was therefore unable to determine how the prevalence rates of depression and anxiety observed in the AS patients compared to those seen in patients receiving radical treatment. Likewise, whilst the findings suggest that AS patients experience a much greater prevalence of anxiety and depression when compared to men of a similar age without PCa, these conclusions are drawn from indirect comparisons with previously conducted research rather than from direct comparison with an age matched control group. It would have been relatively simple to have recruited such an aged matched control group and had I done so it would have provided an important insight into the differing levels of depression and anxiety between these two groups.

Lastly, it was not possible to determine whether the documented distress recorded was a specific result of the patients' PCa diagnosis and treatment with AS or other lifestyle factors. As a postal survey, I had no direct patient contact. Therefore it was not possible to contextualise other stressful life events such as financial problems, relationship breakdowns or family concerns, along with any pre-existing propensity to depression and anxiety, all of which could have equally contributed to the high prevalence rates observed. However it is reasonable to assume that a sample of this size is likely to be fairly representative of the sort of life events that occur to men of this age.

Whilst the cross-sectional design of the current investigation was not able to account for the presence of co-existing life stressors, one of the key inclusion criteria was that participants had to be free from any other significant comorbidity. Whilst I was not able to control for lifestyle stressors, by eliminating men with other serious health conditions I was able to ensure than the high prevalence of distress observed was not due to any other health conditions. I believe that this represents an important strength of the current study.

Another important strength of the current study was the large sample size obtained. Previous investigations into the prevalence of psychological distress in AS patients have been made up of small (n=<150) samples of patients (Burnet et al., 2007; van den Bergh et al., 2009; van den Bergh et al., 2010; Steineck et al., 2002). The only UK based investigation into distress in AS consists of just 100 AS patients in a single centre of national excellence (Burnet et al., 2007). The large number of men recruited into the current study has allowed for the provision of a more reliable and generalisable estimate of depression and anxiety.

Furthermore, previous investigations into psychological distress in AS have typically recruited patients from single sites. This may limit the generaliseabilty of their findings. The 313 AS patients making up the current investigation were recruited from seven independent NHS Trust locations across South, Western and Central England. I believe that in doing so I have increased patient diversity and therefore the generaliseabilty of the findings.

However, in any multicentre investigation it is important to be aware of the issue of clustering. A clustering effect can occur when patients from the same research site display similar characteristics due to their exposure to site specific confounders such as practitioner or clinic effects. In relation to the current investigation, clustering could have occurred in two key ways.

Firstly, it has been documented that patients seeing the same clinician are more likely to receive similar treatment for a given condition than those being treated for the same condition

by different doctors (Steginga et al., 2004). A clinician's preference for varying treatment approaches and their communication skills when articulating such preferences can have a substantial and direct impact upon a patient's psychological and emotional health (Steginga et al., 2004; Steginga et al., 2008). In this way a consultant's communication skills may result in a large practitioner effect being observed; urologists who are encouraging and optimistic about the use and safety of AS are likely to have a reassuring effect upon AS patients. This may increase a patient's acceptance of and belief in AS as their best treatment approach. This is likely to lower rates of psychological distress. Urologists who are in favour of quick radical intervention may be less supportive and encouraging, either consciously or subconsciously, of AS. This may increase uncertainty and anxiety in the patient. It follows therefore that if all of the AS patients at each individual site were being managed by the same consultant, the views of that consultant may have created a large practitioner clustering effect at that site.

Each of the 7 recruiting NHS Trusts in the current investigation had a minimum of four consultant PCa urologists. In the PCa clinics at each of the 7 sites, patients were not allocated to a specific urologist for their appointment. The urologist they saw depended upon which one was free during the time of their appointment. Over the course of their routine follow up it is highly unlikely that any AS patient would see that same urologist at each subsequent appointment. This substantially reduces the likelihood of their being a direct practitioner effect upon a patient's view of, and psychological response to, AS as their chosen treatment approach.

A potential argument against this is that it is common for clinicians and health care professionals from the same department to share similarities in terms of treatment approach preferences. If such a situation was present in the PCa clinics at each of the 7 centres recruiting into the current investigation, it was possible that irrespective of which consultant an AS patient saw, the feedback and advice they would receive would be similar based upon the assumption that all of the consultants would hold similar views of AS. This would again result in a clustering effect.

However, it is again unlikely that this was the case. Within most PCa treatment centres, certainly all of the 7 centres recruiting into the current study, there existed a urologist who specialised in AS and whose key role and clinical interest was in the non-invasive management of PCa. Likewise there were urologists who specialise in the radical treatment of PCa via surgery and hormone therapy. All of these urologists will see, advise and treat AS patients but their views and attitudes towards AS, and the direct and non-direct ways in which those

attitudes are articulated to the patient, will almost certainly vary greatly. It is therefore unlikely that there was a direct practitioner clustering effect as a result of the urology consultants holding similar views of AS.

A second possible clustering effect that was important to be aware of was the possibility that each of the patients attending the same PCa clinic at each of the 7 recruiting centres were geographically, demographically and socio-economically homogeneous. If this were the case, there was a risk of a strong patient clustering effect impacting upon the prevalence data observed. For example, if the patients attending the Weston-Super-Mare PCa clinic were clustered around an affluent area with high education levels, there is the chance that these more educated patients would better understand the clinical rationale for AS, be reassured by this and therefore experience less anxiety as a result.

However, the geographical catchment areas for each of the 7 recruitment centres were very large and in all cases included several large towns and in some cases additional cities. For example, many of patients attending the Southampton clinic resided in Winchester or Portsmouth whilst the Coventry clinic treated patients from both Rugby and West Bromwich. The demographic and socio-economic variation present in such large geographical catchment areas is likely to be very large. This substantially reduces the chances of the PCa clinics at each of the 7 recruitment centres being attended by a demographically and socio-economically homogeneous patient group. Whilst is was important for me to be aware of the impact a patient specific clustering effect could have upon the depression and anxiety data produced, it appears that this effect was likely to be minimal due to heterogeneity associated with the sample of patients attending each of the recruiting PCa clinics.

However, whilst I believe that the geographical, demographic and socio-economic heterogeneity of the patients attending each of the recruitment centres strengthens the generaliseabilty of the findings, it is important to address the ethnical homogeneity of the recruited sample and the limitations that this imposes upon the interpretation of the results.

It was a key aim of the investigation to recruit a sizeable number of AS patients from the Afro-Caribbean community. This would allow me to address the dearth of research conducted into the psychological wellbeing of PCa patients from this ethnic minority group (Dall'Era et al., 2008). This is important as men of Afro-Caribbean decent have an increased genetic predisposition to PCa (Ben-Shlomo et al., 2008). To do so I purposely targeted, approached and

was successful at opening recruitment centres in locations with a high percentage of men from the Afro-Caribbean community (Coventry, Warwickshire and London).

Despite these measures, over 95% of the AS patients recruited into this investigation were of White British origin. This means that I have very little knowledge or understanding of how men from the Afro-Caribbean community respond and cope with a PCa diagnosis and subsequent management with AS. In light of this homogeneity, it is important that the results of the current investigation are not generalised to the high proportion of Afro-Caribbean AS patients.

The primary reason for this homogeneity was that all of the research sites recruiting into this investigation had very low flow rates for ethnic minority patient groups. Unfortunately it was not possible to formally investigate the ethnic make-up of each site as this project, nor the research nurses running the recruitment at their respective sites, had the financial resources or time to do so. However, all of the 7 sites were asked to estimate the ethnic composition of their clinics and all of them estimated that between 15%-25% of their patients were of an ethnic minority group, other than for University College London Hospitals NHS Trust and Coventry and Warwickshire Foundation Trust who estimated this to be around 35%-45%.

A record of the number of Afro-Caribbean men approached at Southampton was kept (2 approached, 0 recruited). However, for logistical reasons I did not ask the research nurses at the other sites to log this information; it required a lot of time and work to open each of the other 6 recruitment sites and in all cases the nurses running the research were over-burdened but agreed to take this investigation on due to the fact that it required minimal work and no face to face patient interaction. It was felt that asking them to track and log the number of patients from each ethnic group approached would have increased the burden upon them and would possibly have jeopardised their willingness to partake. Furthermore as a PhD student we had no funding to employ staff to carry out this data recording. This represents an important limitation of the study but it was one driven by the pragmatic restrictions of running a time and financially restricted project.

It is difficult to know why my attempts to recruit black men were largely unsuccessful. In both the UK and the US, efforts to recruit black men into PCa specific research have been largely unsuccessful with extremely low recruitment and retention rates (Jones et al., 2009). Royal et al (2000) attributed the lack of participation in PCa research among black men to economic limitations, low levels of education, poor access to healthcare, lack of awareness regarding studies, past negative experiences, physicians' attitudes, cultural and religious beliefs and attitudes, and fear of sexual ridicule. Royal et al's (2000) results were derived exclusively from

black men from the US and the absence of UK specific data means it is hard to know how transferable such findings are to the Afro-Caribbean community in the UK.

It is clear from the current investigation that if we are to devise PCa specific research that is going to be successful in recruiting ethnic minority groups, a different recruitment approach will be required. Such an approach should involve contacting religious establishments with a traditionally large black congregation (e.g. the Baptist Church in the UK), black community centres and black PCa specific support charities such as Cancer Black Care. It would seem imperative that future research investigations adopt such approaches to ensure that psychological distress in AS patients from ethnic minority groups is defined and appropriately managed and our clinical approaches are not based upon generic data that is derived almost exclusively from White British men.

4.5.3. Previous Research

In the current investigation a high prevalence of clinical depression and anxiety in men with PCa being managed with AS was observed. Based upon the most recent UK statistics, the prevalence of clinical depression and anxiety in British men aged over 65 is 6% and 8%, respectively (Department of Health, 2011). The current findings suggest that AS patients are over twice as likely to be clinically depressed, and three times as likely to be clinically anxious, as men of similar age in the community.

Similarly, the data generated through the meta-analysis conducted in the previous chapter revealed a depression and anxiety prevalence specifically for men being managed with AS of 9.47% and 16.57%, respectively. Likewise, the on-treatment prevalence data generated generically for men with localised PCa (irrespective of their treatment modality) revealed a depression and anxiety prevalence of 9.7% and 15.17%, respectively. The findings from the current investigation suggest that this cohort of AS patients experienced a slightly higher prevalence of depression and a substantially high prevalence of anxiety than that observed in other AS patients and generic PCa patients with localised disease.

The clinical implications of these findings are of great significance to the burgeoning population of AS patients in the UK. Elevated anxiety has been shown to act as an independent predictor of men on AS progressing to radical intervention in the absence of clinical evidence of disease progression. Patel et al., (2004) observed that almost 10% of AS patients opt for radical intervention because of the anxiety they experience as a result of living with an "untreated" cancer. In all cases none of the men had or were displaying any clinical evidence

of disease progression. Likewise, Latini et al., (2007) observed that cancer anxiety represented the most significant predictor variable of men on AS opting for radical intervention in the absence of disease progression.

Recent longitudinal research has conclusively shown that for men with localised, slow growing PCa, radical intervention in comparison to observation is not associated with a significant increase in 12 year survival (Wilt et al., 2012). Yet men opting for radical intervention experience a 28% and 35% greater risk of long term incontinence and impotence respectively (Wilt et al., 2012). Incontinence and impotence within this patient group is significantly correlated with reduced quality of life (Bisson et al., 2002; Ene et al., 2006).

Managing these vulnerable AS patients so they are less likely to opt for clinically unnecessary radical intervention should be an area of key focus for health care professionals working within the field of PCa as a means of optimising patient quality of life and limiting the physical side effects associated with radical treatment. Such an approach also has potentially large and positive economic ramifications and could save the NHS substantial amounts of money through reduced unnecessary surgical interventions.

Such a stance is completely in keeping with the National Cancer Survivorship Initiative's survivorship framework which stresses the importance of selecting treatment approaches that not only maximise survival but also prioritise the preservation of quality of life (National Cancer Survivorship Initiative, 2010). It is hoped that the results of the current investigation will go some way in informing those working with AS patients of the high prevalence of depression and anxiety in this patient group so that such conditions can be better diagnosed and managed.

To date, the only other study to specifically assess depression and anxiety prevalence in PCa patients being managed with AS in the UK was conducted by Burnet and her colleagues (2007) from the Royal Marsden Hospital in London. Their results concluded that the prevalence of psychological distress in patients being managed with AS was not significantly higher than in patients receiving radical intervention. The interpretation of these results is misleading. In their study, patients being managed with AS experienced a prevalence of clinical anxiety over twice that of patients being treated radically (21% and 10% respectively). Such findings clearly suggest that AS is associated with far higher rates of psychological morbidity than radical treatment interventions. Unfortunately these findings did not reach statistical significance due to small sample sizes. This does not mean that the results are not of clinical importance but rather they have been interpreted incorrectly.

Based on the findings of Burnet et al., (2007), men being managed with AS are almost three times as likely to be experiencing clinical anxiety as men aged over 65 in the community (Department of Health, 2011) and more than twice as likely to be anxious as men being treated radically. Yet in too many cases, subsequent investigations have cited Burnet et al's (2007) findings to support the notion that AS does not predispose patients to a greater risk of psychological distress (Thong et al., 2010; Goh et al., 2012). The outcome of this is that health professionals working with AS patients are likely to be making treatment decisions based on a misinterpretation of Burnet's data. Burnet's conclusions do not portray a clinically accurate picture of the prevalence of psychological morbidity within this patient group because the authors have not taken into account the limitations of their sample size and its impact on the subsequent analysis.

Furthermore, participants taking part in the Burnet et al (2007) investigation were recruited exclusively from the Royal Marsden Cancer Centre. This institution is a world leading cancer treatment centre and a global authority on the diagnosis and management of cancer. Cancer patients being treated at the Royal Marsden receive an unparalleled level of support. Such high levels of patient care would undoubtedly have a positive impact upon lowering psychological distress and concern. The participants recruited by Burnet are unlikely to be representative of UK cancer management and it is possible that AS patients being managed in locations other than the Royal Marsden may display higher levels of psychological distress.

Burnet's findings are interesting and important but are being misinterpreted due to their limited sample size. If it were possible to collectively pool together and meta-analyse the individual patient data sets from both Burnet's investigation and my own, we would have a sample of over 400 AS patients. This would increase the likelihood of finding a statistically significant difference in the prevalence of clinical depression and anxiety in AS patients in comparison to those undergoing radical intervention in Burnet's dataset. This would allow for the more accurate interpretation of Burnet's findings and ensure that health care professionals working in the field of PCa receive the best evidence regarding the elevated risk of psychological distress in men being managed with AS. Access to this information would inform treatment decision making, increase patient's treatment centred health literacy and ensure than men being placed onto a AS protocol do so in full knowledge of the associated psychological risks.

To address this issue I have contact Dr Chris Parker who is a consultant oncologist at the Royal Marsden and lead clinician on the Burnet investigation. I asked Dr Parker if he would be willing

to work with me in a collaborative manner to allow us to pool together our two individual data sets and analyse this meta-analytically. If this approach is successful, we will be able to produce an even larger and more definitive estimate of depression and anxiety prevalence in AS patients. By increasing the pooled sample size to 413, it would be possible to increase the ability to estimate the proportion of men who are depressed and anxious using a 95% confidence interval to within 2.6%

The current investigation has also illuminated several avenues of future research than may be fruitful in allowing us to further our understanding of the causes of psychological distress within the AS community. The results generated from the analyses of the demographic data revealed that NHS Trust site was the only demographic variable significantly associated with depression. More specifically, men recruited from Southampton University Hospitals NHS Trust and Mid-Essex NHS Trust Foundation had a higher prevalence of depression than did men from the other five NHS Trusts. However, of the collective sample of 313 participants recruited into the study, only 28 and 14 men were from recruited from Southampton and Essex, respectively. It is likely that this finding may be a direct result of small sample sizes rather than any site specific socio-demographic variables inherent to Southampton and Essex as geographical entities.

Despite this statistical limitation, it is still possible that NHS Trust site as a demographic variable may have an important impact upon the prevalence rates of psychological distress observed. PCa diagnostic procedures vary widely across NHS Trusts. This is particularly true in regards to the monitoring of disease progression in men with localised and stable PCa who are being managed with AS. In the majority of Trusts, patients on AS undergo an initial template biopsy followed by routine PSA screening.

AS patients have little faith in the diagnostic accuracy of PSA monitoring (Martin et al., 2006). Indeed, research evidence would suggest that fears of unchecked disease progression as a direct results of the inaccuracies of PSA monitoring is one of the predominant concerns of patients on AS (Latini et al., 2007; Patel et al., 2004; Hedestig, Sandman & Widmark, 2003). AS patients being treated in NHS Trust sites that rely exclusively on PSA tests to monitor disease progression may be at an increased risk of psychological distress due to their concerns about the perceived inaccuracies of this approach and the fear that disease progression may go unchecked.

In contrast, several Trusts now utilise more sophisticated imaging technology, such as MRI scanning, to more definitively map PCa volume and progression rates. It is possible that more

advanced imagining technologies, such as MRI, may provide an effective method of alleviating psychological distress; if urologists are able to show AS patients their MRI images to let them visually see the lack of progression in scans that were taken 12 months apart, it may help AS patients to rationalise, process and accept the slow growing indolent nature of their condition. This in turn may help lower psychological distress and so reduce the rate of anxiety induced transference to unnecessary radical intervention.

Whilst sample size limitations may be responsible for the higher rates of distress prevalence observed at Southampton and Essex, it is still plausible that local disease monitoring processes may have a direct impact upon the prevalence of psychological distress observed. Interventions that are effective at alleviating fears of unmonitored disease progression may provide an effective method of lowering depression and anxiety in AS patients. This points to the possibility of using more advanced diagnostic and monitoring techniques, such as MRI, to increase patients acceptance of AS and to alleviate their fears of unchecked disease progression. Further research into how the disease monitoring processes impacts upon distress is warranted.

4.5.4. Conclusion

The aim of this study was to generate a more definitive estimate of the prevalence of depression and anxiety among a large sample of AS patients from within the UK. The results have highlighted that AS patients display a high prevalence of depression and anxiety which is substantially greater than that observed in the general population of men of a similar age in the UK (Department of Health, 2011).

It was also my aim to determine whether any patient demographic variables were significantly associated with depression and anxiety prevalence. The cross tabulations highlighted only two such variables; NHS Trust site was significantly associated with a higher number of depressed patients whilst relationship status (divorced) was associated with a significantly higher number of anxious patients. However, in both cases these results are most likely due to small sample sizes. The logistic regression analyses failed to identify any demographic variables that were able to significantly predict depression and anxiety. Whilst the current study is the largest of its kind to assess depression and anxiety among AS patients, it is likely that to effectively identify any demographic variables that are predictive of psychological distress, a far larger sample size would be needed.

Previous studies into the measurement of depression and anxiety in AS patients have recruited patients from single sites (Burnet et al., 2007; van den Bergh et al., 2009; van den Bergh et al., 2010; Steineck et al., 2002). To address this issue it was also my aim to recruit patients from multiple NHS Trust locations across the UK. It was my hope that doing would increase the generaliseabilty of the findings. Through opening up recruitment centres at seven independent NHS Trusts across South, Central and Western England, I feel that I have generated a more robust, accurate and generalisable estimate of depression and anxiety prevalence in AS patients in the UK.

In conclusion, this study has observed that AS patients experience a high level of depression and in particular anxiety. Anxiety is currently one of the most significant independent predictors of men on AS opting for radical intervention. In a bid to minimise anxiety and so lower this rate of transference, there currently exists a need for the development and implementation of support interventions that will equip AS patients with the tools and techniques that will allow them to better manage the uncertainty of AS and so reduce anxiety and subsequent transference to radical treatment.

One potentially fruitful means of doing so may be through the use of self-care techniques such as Mindfulness Based Stress Reduction (MBSR). One posits that teaching AS patients the core components of MBSR would help ground them in the present moment and allow them to better cope with and recognise the largely subjective ruminative thoughts and processes that appear to be the main cause of distress in this patient group (Hedestig, Sandman & Widmark, 2003; Kronenwetter et al., 2005).

The paucity of evidence relating to the use of MBSR specifically in PCa meant that it was not possible to run a literature review specifically within this area to allow me to better assess the feasibility of using an MBSR intervention in a sample of AS patients. To help address this issue and provide some insight into PCa patients' use and acceptance of general self-care interventions, it was decided upon to run a broader literature review which assessed the current base of evidence relating to PCa patients involvement in self-care interventions and the effect such interventions have at managing psychological distress in this patient group.

Chapter 5

A Narrative Literature Review of Self-Care Interventions for the Management of Psychological Distress in Men with Prostate Cancer.

5.1. Research Objectives:

1. To determine the extent of the evidence base for the use of self-care interventions in men with PCa.

2. To determine whether self-care interventions in men with PCa are effective at improving psychological health and wellbeing.

3. To determine whether self-care interventions in men with PCa have utilised group based support and if so whether they have been able to effectively recruit patients into such interventions.

4. To assess whether any investigations have attempted to utilise mindfulness based interventions in men with PCa and if so were they able to recruit patients to trial, did the patients adhere to the intervention and was the intervention effective.

5.2. Introduction

The findings from the cross-sectional survey of depression and anxiety prevalence overviewed in the previous chapter clearly highlighted that men being managed with AS experience a high degree of psychological distress. AS patients represent a burgeoning patient group that experience good long term survival but the depression and anxiety they commonly experience is currently not being managed in a systematic and effective manner. It is important that measures are taken to address this issue.

Yet within the field of PCa, it has been shown that physicians are in many instances not able to address and advise on men's psychological, emotional and supportive care needs when they are raised (Brown et al., 2003). Hence it seems unlikely that the support PCa patients require will arrive directly from their clinical care team. Other approaches are therefore needed. Health care services around the world, including the NHS, are under increasing economic pressure to find ways of reducing expenditure. Any supportive services offered to PCa patients to help them better manage the psychological and emotional consequences of their condition must be not only clinically effective but also economically viable and sustainable. One approach that may offer a potentially effective means of doing so is self-care interventions.

Self-care interventions encompass a heterogeneous range of approaches and techniques that aim to educate, equip and empower patients with a variety of skills, tools and techniques that will allow them to better cope, manage and live with the psychological, emotional and physical side effects of their condition (Barlow et al., 2002). The foundation of evidence into the design and assessment of self-care interventions in chronic conditions outside the realm of cancer is extensive (Cockle-Hearne & Faithful, 2010). Less evidence currently exists specifically for cancer survivorship but that which does exist has already had a substantial influence upon the reformulation of cancer management and survivorship policy in the UK to ensure that the psychological and emotional consequences of survivorship are not dismissed (Department of Health, 2006 & 2007).

Perhaps unsurprisingly, the majority of research into the design, development and implementation of self-care interventions within cancer have been conducted within the confines of breast cancer (Kissane et al., 2007; Guo et al., 2013; Cimprich et al., 2005). The evidence from these investigations suggest that self-care interventions are effective at lowering depression and anxiety, increasing functional quality of life, improving mood, enhancing self-efficacy and increasing coping ability. However, the variety of these self-care interventions in terms of their structure, format, content and setting vary drastically. For example, they have been conducted in group settings and on a one-to-one basis (Thompson et al., 2013; Badger et al., 2000). They have been implemented by psychologists, nurses, social workers, expert patients and lay instructors (Bloom & Stewart, 2008; Thompson et al., 2013; Badger et al., 2000; Fenlon & Foster, 2009) and have been offered remotely via a multitude of mediums that include websites, email, mobile apps, telephone support and mailed hard copy information packs (Hawkes, Gollschewski & Chambers, 2009; van den Bergh et al., 2012; Schulman-Green & Jeon, 2013; Cimprich et al., 2005).

The last several years have seen an increasing focus and drive into the design and assessment of self-care interventions specifically within PCa. These have also varied greatly in terms of their structure, content and mode of delivery (Parker et al., 2009; Bailey et al., 2004; Kazer et al., 2011).

As one of the aims of this PhD was to investigate the effectiveness of a self-care intervention in the form of a group based MBSR intervention to manage depression and anxiety, I wanted to assess and review the available research into the use of self-care interventions specifically

within the realm of PCa. Doing so would allow me to more accurately determine the likelihood of the planned group based MBSR investigation being positively received by, recruited into and adhered to by a group of PCa patients being managed with AS.

Whilst assessing the literature relating to the use of self-care interventions among PCa patients, it became apparent that the research could best be categorised by the means in which the interventions were delivered to patients. These fell into four distinct categories:

1. Self-care interventions that were delivered in a group based environment.
2. Self-care interventions that were delivered over the telephone.
3. Self-care interventions that were delivered over the internet.
4. Self-care interventions that were delivered by any other means.

Each of these categories will be reviewed individually before providing a summary discussion of the evidence both collectively and in context.

5.3. Methods

Narrative literature reviews utilise a different methodology to systematic reviews. Systematic reviews seek to answer clearly formulated research objectives by using rigorous, explicit protocols to identify, select and appraise relevant research studies and to collect and analyse data from these. To minimize bias, they include or exclude evidence on the basis of explicit quality criteria. The outcomes generated through systematic reviews constitute evidence.

In contrast, narrative reviews articles may be evidence-based, but they are do not constitute evidence and are traditionally performed to provide a detailed overview of the evidence in a specific area of research.

However, the confidence that one can have in the conclusions drawn from a narrative review can be enhanced by adopting a methodology that ensures that the research aims of the review are effectively addressed whilst ensuring that all of the key research within the area has been identified and analysed. Therefore whilst it is not always necessary to develop a specific data searching strategy for a narrative review, doing so constitutes good practice and enhances the rigour of the review.

5.3.1. Eligibility criteria

Study Design:

- Primary research studies published in full journal articles that investigated the utilisation of self-care interventions for the management of psychological distress specifically in PCa were eligible for inclusion.
- Studies published in conference proceedings, commentaries and discussions, letters, books, book chapters or research not published in the English language were excluded.

Population:

- The current review was restricted to research focusing on individuals with PCa.
- If PCa patients were included within an investigation that recruited mixed cancer populations, the study was required to have reported data about the PCa patients as a distinct sub-sample.
- Where research included both the PCa patients and their spouses/partners in the investigation, the study had to report data about the PCa patients as a distinct sub-sample.

5.3.3. Identifying Research Evidence

To maximise the diversity and scope of the literature search in the current review and to minimise the degree of publication bias encountered, multiple search strategies were utilised, all of which are overviewed below.

- **Search Strategy Validity**

Electronic Database Searches

I searched six electronic databases for articles that met the above specified inclusion criteria using pre-specified search terms as listed in Table 29 below:

Table 29: Databases, Date Ranges and Search Terms Used to Identify Relevant Articles

Database	Date Range Searched	Search Terms
Ovid Medline	1950-2010	MeSH terms: Prostate Neoplasm (EXP)" OR "Prostate Cancer" AND "Depression (EXP)" or "Anxiety (EXP)"
EMBASE	1980-2010	Free Text Key Words: "Prostate Neoplasm" or "Prostate Cancer" AND "self-care" or "self-management" or "self-help" or "support groups" or "group support interventions" or "psychological

		distress" or "meditation" or mindfulness based stress reduction" or "MBSR" or "telephone support" or "internet support" or "internet interventions" or "nurse interventions" or "nurse support".
AMED (Allied and Complementary Medicine)	1985-2010	Free Text Key Words: "Prostate Neoplasm" or "Prostate Cancer" AND "self-care" or "self-management" or "self-help" or "support groups" or "group support interventions" or "psychological distress" or "meditation" or mindfulness based stress reduction" or "MBSR" or "telephone support" or "internet support" or "internet interventions" or "nurse interventions" or "nurse support".
PsycINFO	1985-2010	Free Text Key Words: "Prostate Neoplasm" or "Prostate Cancer" AND "self-care" or "self-management" or "self-help" or "support groups" or "group support interventions" or "psychological distress" or "meditation" or mindfulness based stress reduction" or "MBSR" or "telephone support" or "internet support" or "internet interventions" or "nurse interventions" or "nurse support".
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982-2010	Free Text Key Words: "Prostate Neoplasm" or "Prostate Cancer" AND "self-care" or "self-management" or "self-help" or "support groups" or "group support interventions" or "psychological distress" or "meditation" or mindfulness based stress reduction" or "MBSR" or "telephone support" or "internet support" or "internet interventions" or "nurse interventions" or "nurse support".
Web of Science	1970 – 2009	Free Text Key Words: "Prostate Neoplasm" or "Prostate Cancer" AND "self-care" or "self-management" or "self-help" or "support groups" or "group support interventions" or "psychological distress" or "meditation" or mindfulness based stress reduction" or "MBSR" or "telephone support" or "internet support" or "internet interventions" or "nurse interventions" or "nurse support".

Reference List Searches

- To supplement the electronic database searches, I also conducted searches of the reference lists of previous reviews, key papers and relevant articles identified by the electronic search.

I also conducted comprehensive hand searches of my personal files and other relevant papers not identified electronically to increase the likelihood of identifying relevant articles published in journals not indexed electronically.

5.3.4. Study Selection

Study selection followed an iterative process that began with collating, reading and critically appraising all the abstracts identified by the electronic, reference list and hand searches. If it was possible to confirm from the abstract alone that an article was not suitable, it was immediately rejected. All articles that appeared suitable were retrieved in full for further analysis.

All of the retrieved full text articles were then read in full to determine which studies were acceptable for entry into the narrative review.

5.3.5. Data Analysis

All suitable studies were classified into the following categories to allow for the more coherent and consistent interpretation of their findings:

5. Self-care interventions that were delivered in a group based environment.
6. Self-care interventions that were delivered over the telephone.
7. Self-care interventions that were delivered over the internet.
8. Self-care interventions that were delivered by any other means.

Once all of the included studies had been classified into the above categories, the review of each individual article could begin. Each article was assessed and analysed individually and the pertinent data extracted; due to the heterogeneity of the included studies, an extraction spreadsheet (as would be utilised for a systematic review) was not deemed suitable.

5.4. Results

5.4.1. Self-care interventions that were delivered in a group based environment

The majority of self-care interventions that have been investigated within PCa have been offered as group based interventions. These can be further categorised into those that 1) offered stress management and relaxation skills and 2) those that offered disease specific information and education to improve patient health literacy alongside stress management and relaxation skills. Each of these will be addressed in turn.

5.4.1.1. Stress management and relaxation based group interventions

Several investigations have aimed to assess the effectiveness of stress management interventions at improving psychological health and wellbeing among PCa patients. In one of the most recent attempts to do so, Parker et al., (2009) developed a brief pre-surgical stress management intervention for PCa patients scheduled to undergo radical prostatectomy. This represents a novel avenue of research as it is one of only a few interventions within the generic cancer research that has attempted to address psychological health pre-treatment; much of the research into self-care interventions among cancer patients has focused on the on-treatment and post-treatment phase (Cimprich et al., 2005; Badger et al., 2003; Thompson et al., 2013). The rationale for doing so was that the pre-treatment phase is often associated with substantial psychological dysfunction which is largely unmet. Furthermore, patients who are provided with stress management techniques prior to surgery report reduced pain and distress, improved quality of life, require less pain medication and have lower systolic blood pressure (Manyande et al., 1992; Manyande, Berg, & Gettings, 1995; Kshettry et al., 2006).

In their study, Parker et al., (2009) assessed the effectiveness of a stress management intervention against a brief psychological consultation and a control group. The stress management intervention consisted of two 90-minute sessions in which the patients were instructed in the use of relaxation skills such as diaphragmatic breathing, body scans and guided imagery. Patients were also guided through an imaginal rehearsal of what would happen and what to expect on the morning of their surgery to help forewarn and thus forearm them of the likely procedures. They postulated that doing so would help lower anxiety. Patients also discussed their fears and concerns and learnt how to design and implement coping strategies. The patients also had two brief “booster” sessions on the morning of their surgery and 48 hours post-surgery.

The results indicated that in the week before surgery, the patients attending the stress management sessions has significantly less mood disturbance, reduced physical side effects and less cancer related worry than patients in the other two groups. Interestingly, these effects were maintained at 12-month follow up. This suggests that either the skills the patients learnt during the intervention had a long lasting effect or that the patients continued to independently practice and utilise the skills during the 12-months after the completion of their surgery. This suggests that in newly diagnosed PCa patients who were due to undergo surgery,

stress management and relaxation skills training had a significant impact upon improving pre and post-surgery psychological and physical health and wellbeing.

Interestingly, one of the rationales for the utilisation of a brief (two session) intervention in the Parker investigation was that its brevity would make the intervention more appealing to PCa patients and thereby increase recruitment and adherence. This rationale appears to be supported; out of an approached sample of 221 men, 159 were successfully recruited into and completed the investigation. These data suggest that PCa patients are interested in and willing to recruit into a self-care intervention that aimed to equip them with skills to better manage their psychological distress.

The fact that the intervention offered by Parker included breathing based relaxation techniques is encouraging and suggests that approaches such as these may be deemed acceptable to PCa patients. This is an important issue given that it was my desire to offer a breath based MBSR intervention to PCa patients. However, the intervention offered by Parker was extremely brief in comparison to the more time demanding 8-week intervention that makes up a standardised MBSR programme. It may be that PCa patients would be less inclined to recruit into self-care interventions that require such a substantially more demanding time commitment.

Whilst such a stance appears plausible, two investigations conducted by Penedo et al., (2004 & 2006) suggest that this is not the case. In their study, they aimed to investigate the effectiveness of a 10-week cognitive-behavioural stress management (CBSM) intervention on quality of life in men who had been treated by radical prostatectomy or radiotherapy for localised PCa. The CBSM intervention involved a group of 10 patients meeting once per week for two hours over a ten week period. A large portion of this time was spent on breath and muscle based relaxation techniques. Other approaches used included identifying distorted thoughts and beliefs, coping strategies, goal setting and utilising social support.

The results revealed than men undertaking the CBSM intervention displayed significant improvements in both general and PCa specific quality of life indices in comparison to the patients assigned to the control group. It was also revealed that these significant improvements were directly mediated by increases in patient reported stress management

skills. This again suggest that in PCa patients, breath based relaxation interventions are both well received and clinically effective.

Relating specifically to this PhD, the findings highlighted by Penedo are important. The CBSM intervention offered by Penedo was 10-weeks in duration and consisted of over 20 hours of group contact time. This is longer and more time demanding than the MBSR intervention I hoped to trial in the current PhD which consisted of an 8-week programme constituting 16 hours of group contact. Crucially, Penedo was able to successfully recruit just under 100 patients (n=96) into the CBSM intervention. Whilst the absence of any response rate data means that it is not possible to determine how many eligible patients were approached to reach this figure , these findings still suggest that a prolonged time demanding group intervention that focuses predominantly on breath based relaxation training is deemed acceptable enough to PCa patients to warrant their time investment in it.

This is a view supported by Carlson et al., (2003 & 2007) who conducted the only investigations to date to have recruited PCa patients into a standardised MBSR intervention. In this longitudinal study, Carlson investigation into the impact of a standardised 8-week MBSR intervention on quality of life, psychological health, mood, fatigue, sleep and a variety of immune and endocrine markers in a mixed sample of cancer patients, including PCa patients. The results highlighted that taking part in the MBSR intervention was associated with significant improvements in sleep disturbance, sleep quality, stress levels, anxiety, mood disturbance and fatigue. It is encouraging that Carlson was able to recruit PCa patients into a MBSR investigation but these findings must be treated cautiously. Across the investigation, PCa patients made up less the 6% (n=16) of the total sample size. Unfortunately no response rates were provided which meant it was not possible to ascertain how well received the MBSR intervention was by the collective pool of PCa patients who were approached for entry into the investigation.

Furthermore, Carlson failed to stratify the generated findings as a function of cancer site. The majority of patients recruited were breast cancer patients (69%). It could be that the positive results obtained were generated almost entirely by these women and not by the PCa patients whose numbers were too small to impact upon the significance of the findings. As these studies are the only ones of their kind to recruit PCa patients, it is currently not possible to determine how effective MBSR will be within this patient cohort. Yet despite this, the findings

observed by Parker et al., (2009), Penedo et al., (2003 & 2006) and Carlson et al., (2003, 2007) suggest that group based support which focuses on equipping PCa patients with the tools to better manage psychological distress are well received by men in this patient group.

Indeed the perceived benefits of and acceptance towards group based self-care interventions within PCa was comprehensively investigated by Steginga et al., (2005) who conducted a large national survey of PCa patients' evaluation of the benefits of attending group based support. Whilst this study did not have an interventional component it nevertheless provided invaluable information into the potential benefits afforded to PCa patients by attending group support.

Across a combined sample of 1224 patients, their survey revealed that 61% of men were very satisfied and 21% satisfied with the services and benefits obtained by attending their support group. Furthermore, among these 82% of patients, satisfaction with group support was significantly associated with a higher quality of life. These findings add further support for the assumption that PCa patients are both willing to recruit into and attend group support sessions and find substantial satisfaction and benefit in doing so.

5.4.1.2. Informational and educational group interventions

It has been identified that following a diagnosis of PCa, one of the greatest fears experienced by patients is fear of the unknown and uncertainty about the future, treatment, side effects and mortality (Dale et al., 2005). One potential means of combating this is through the effective provision of information and education. Indeed, among breast cancer patients the desire for disease specific information is viewed as an essential and fundamental form of support (Brown, Koch & Webb, 2000). Consequently several studies have attempted to assess the effectiveness of group based interventions as a means of imparting such information to PCa patients as a means of targeting psychological dysfunction.

Templeton & Coates (2004) designed a brief single session, group based, nurse led informational intervention for PCa patients being treated with hormone therapy. The group session was supported by a comprehensive hard-copy PCa information booklet which provided detailed information about PCa and hormone therapy. Their results indicated that in comparison to the control group, the PCa patients undertaking the group session displayed a

significant improvement in general and PCa specific quality of life, PCa knowledge and satisfaction with care.

The results of the Templeton & Coates (2004) investigation are interesting as they suggest that a very brief group based intervention was able to produce significant improvements in quality of life and PCa knowledge. Unfortunately no longitudinal follow-up was undertaken which means it was not possible to determine whether these effects were maintained for any meaningful period of time. Yet these findings suggest that the effectiveness of group based interventions for PCa may not be dose related and that brief interventions may offer equal effectiveness to longer more time demanding ones.

Shorter interventions such as those offered by Templeton & Coates (2004) also have additional benefits; they may be associated with better rates of patient uptake due to reduced commitment and time demands and they also offer greater value for money. However, the Templeton & Coates (2004) investigation did not measure and assess anxiety and depression as specific psychological conditions. Consequently it is not possible to determine whether an information only intervention such as this would have any meaningful effect at improving anxiety and depression in the absence of any stress-management or relaxation specific techniques.

This was the case in an investigation conducted by Berglund et al., (2007) who assessed the effectiveness of a 7-week group based intervention on depression, anxiety and quality of life in a large sample of PCa patients. The intervention consisted of an information arm, a physical activity arm and an information and physical activity combined arm. The information only group was led by a PCa nurse practitioner who overviewed what PCa was, how it can be treated, benefits, risks and side effects of different treatment options and methods of dealing with urinary and sexual dysfunction. The physical activity group was led by a physiotherapist and focused on increasing daily exercise levels, overviewing the benefits of exercise during cancer treatment and survival and on strengthening pelvic floor muscles. The information and physical activity combined group received both of the above. A control group was also utilised which received standard care.

The results indicated that none of the groups had any significant effect on improving depression and anxiety (as measured by the Hospital Anxiety and Depression Scale) or quality of life in comparison to each other or the control group. These findings are in stark contrast to the results obtained by Templeton & Coates (2004) who showed that just one single group session was sufficient to produce a significant increase in PCa related quality of life.

It is difficult to understand why the 7-week intervention was ineffective. The authors hypothesised that they expected the information arm to experience a reduction in anxiety and the physical activity arm a reduction in depression. Whilst information provision has often been shown to help alleviate anxiety among cancer patients, it has usually been offered alongside relaxation based skills training (Newell et al., 2002; Okamura et al., 2003). Doing so allows the patients to address both the causes of the anxiety (i.e. lack of information) and the symptoms of it (i.e. nervousness, fear, agitation). Because Berglund only provided information and not relaxation, it may have been that despite the patients becoming more informed about PCa and its treatment, they were still unable to effectively manage the symptoms of their anxiety.

Finally, only one study to date has investigated the effects of a group based intervention that addressed both information provision and relaxation training on quality of life and psychological health in PCa patients (Lepore et al., 2003). This intervention consisted of six weekly 1-hour group sessions that covered prostate cancer biology, treatment options, managing side effects, diet and nutrition and stress, coping and relaxation. Three intervention arms were utilised; intervention only, intervention with a discussion group and a control group.

Their results indicated that across a large sample of post-treatment patients, (n=250) men in both intervention arms (intervention and intervention plus discussion) showed a significant improvement in PCa knowledge and experienced less sexual dysfunction but this was not associated with any significant improvement in depression in comparison to the control group. These findings suggest that a multifaceted group based PCa intervention that addresses both information provision and relaxation is ineffective at improving depression.

However, care must be taken when interpreting these results. Firstly, the baseline assessment of depression occurred at the start of the intervention (after treatment had been completed)

and again at the end of the 7-week intervention. The baseline levels of depression, (as measured by the Centre for Epidemiologic Studies Depression Scale) were extremely low for all groups. Interviews with the patients revealed that this was because they felt their treatment had "cured" them, that they had beaten their cancer and that they would make a full recovery. Therefore the intervention may have been ineffective at lowering depression simply because baseline levels were so low in the first place. The authors suggest that if the baseline measure had been taken pre-treatment, before the patients believed they had been cured, depression levels would likely have been much higher. If this had been the case, the intervention may have shown some effect at lowering depression.

Collectively, the above has revealed that an ample foundation of evidence exists to support the use of group based self-care interventions among PCa patients. The studies have also highlighted that group based self-care interventions that utilise stress management, relaxation training and informational support offer a degree of effectiveness at managing psychological distress in PCa patients. They have also shown that recruitment rates into such interventions are good. In light of my aim to trial an 8-week group based MBSR intervention among a group of PCa patients, these findings were reassuring.

5.4.2. Self-care interventions that were delivered over the telephone

Several investigations have utilised tele-based interventions as a means of offering psycho-educational self-care interventions to PCa patients (Bailey et al., 2004; Chambers et al., 2012). The primary rationale for this was that such approaches are extremely cheap to run, don't require the design, development and maintenance of expensive websites and allow for direct interaction between the patient and a trained specialist.

Interestingly, one telephone intervention has focused specifically on patients being managed with watchful waiting (WW; Bailey et al., 2004). Whilst WW represents a subtly different management approach to AS, both involve the passive management of PCa and both utilise the same process of disease monitoring, that is PSA testing, biopsies and imaging. Indeed, the similarities between AS and WW are such that in many cases the research has used the independent terms interchangeably (Steineck et al., 2002; Pickles et al., 2007). Whilst WW patients will differ from AS patients (they will be older), clinically they are a homogeneous group. This would suggest that the investigation conducted by Bailey et al., (2004) was directly

relevant to and comparably with men being managed with AS and thus of relevance to the work making up the current PhD.

The tele-based intervention offered by Bailey et al., (2004) consisted of 5 brief telephone consultations with a male PCa nurse over a five week period. During the intervention patients were taught how to positively reframe negative thought patters, manage uncertainty, increase acceptance of WW as a preferable treatment approach to radical intervention and to increase self-monitoring and vigilance strategies. The results revealed that the patients who took part in the intervention experienced significant improvements in quality of life and uncertainty management in comparison to controls who received standard care. Likewise, they also experienced a near significant reduction in depression.

It has been shown that among PCa patients being managed with AS or WW, the predominant causes of distress include uncertainty, fears of disease progression and the inherent belief that radical treatment would be a better approach (Hedestig, Sandman & Widmark, 2003; Kronenwetter et al., 2005). It is therefore unsurprising that receiving verbal information from an expert PCa nurse practitioner about how to manage uncertainty and why WW was a better treatment approach to radical intervention acted as an effective means of reducing uncertainty and increasing quality of life.

However, important limitations exist within the Bailey investigation that must be taken into account. Firstly, a high level of homogeneity was observed in their sample; they were largely Caucasian, were recruited from the same clinic and were all being treated by the same physician. Secondly, the patients receiving the intervention had been managed with WW for an average of 4-years. It is likely that over this period of time the patients would have adjusted to the concept of being passively managed and as such would likely be experiencing substantially less psychological dysfunction. The lack of any follow up investigations means that it is difficult to know whether the intervention designed by Bailey would be equally effective in a demographically heterogeneous group of WW patients who were within the first year of diagnosis, a time when psychological distress is generally highest (Pickles et al., 2007).

Indeed, a recent investigation utilising an intervention very similar to that offered by Bailey et al., (2004) revealed that its effectiveness was largely dependent upon the demographic characteristics of the patients using it (Chambers et al., 2012). Like Bailey et al., (2004),

Chambers offered a five session telephone intervention to PCa patients that covered cognitive reframing, education about PCa, managing side effects, stress management and developing problem solving skills. The results revealed that the intervention was significantly effective at improving mental health and lowering levels of cancer related distress but only among PCa patients who were younger and had a higher level of education and income. Conversely, younger men with a lower level of education and income experienced a decrease in cognitive judgement over the course of the intervention.

These results suggest that a brief telephone based self-care intervention is not effective at improving the psychological wellbeing of PCa patients when applied to a heterogeneous sample. The findings of Chambers et al., (2012) appear additionally robust given the large number of patients they recruited (n=740) from multiple centres in relation to the demographically homogeneous sample recruited by Bailey et al., (2004). The absence of any other research utilising tele-based support interventions among PCa patients makes it hard to ascertain the potential effectiveness of this form of support. Additional research to help address this issue would be beneficial, especially in light of the economic benefits afforded by remote interventions of this nature.

5.4.3. Self-care interventions that were delivered over the internet.

Despite the recent increase in research into the use of internet interventions within the health care setting (Webb et al., 2010; Yardley et al., 2011), only two such interventions targeting psychological health specifically in PCa currently exist. Interestingly, one of these was developed specifically for men on AS.

The “Alive and Well” intervention (Kazer et al., 2011) was designed as a psycho-educational cognitive reframing and self-management resource to help men being managed with AS to better cope with uncertainty and improve quality of life. The intervention comprised of 4 components: 1) cognitive reframing strategies to help patients avoid negative thought patterns and maintain a positive outlook, 2) a PCa and AS information section, 3) advice on diet, exercise, weight control and smoking cessation and 4) tailored emails designed to address the specific needs of individual patients. The intervention lasted for 5 weeks and measures of self-efficacy and quality of life were collected at the start, end and 5-weeks after the completion of the intervention. No control group was utilised in this pilot intervention.

The results of the Alive and Well intervention revealed a significant improvement in 8 of 12 quality of life subscales as measured on the University of California-Los Angeles Prostate Cancer Index (UCLA-PI; Litwin et al., 1998). Furthermore, it was revealed that the number of web pages on the internet intervention that were viewed was significantly correlated to two quality of life indices; role function related to emotional health and social function. This would suggest a directly mediated effect between participation in the online intervention and improvement in PCa specific quality of life. The authors also reported that the participants adhered well to the intervention with participants averaging 20 page views over the duration of the intervention.

Unfortunately the benefits observed in quality of life were not sustained and returned to baseline by the time of follow up five weeks later. This suggests that the benefits obtained by the participants as a result of participation in the online intervention were not sufficient to induce more deep seated and robust changes in health behaviour (diet, sleeping and exercise) nor positive thinking patterns and reframing practices. The authors recommended that additional remote support via email, telephone or text messaging may be required to help maintain post-intervention quality of life.

It was also of note that the AS patients recruited into the Alive and Well intervention had been managed with AS for an average of 3 years. AS patients tend to experience the greatest degree of psychological dysfunction in the first 6-18 months post-diagnosis (Pickles et al., 2007). After this period patients tend to adapt well to AS. It is possible that the patients recruited into the Alive and Well investigation would have been experiencing less psychological dysfunction than their counterparts who are in the first 6-18 months of management with AS. Trialling the Alive and Well intervention in a sample of newly diagnosed AS patients would be beneficial to determine whether it would still induce positive alterations to quality of life. However, these early positive findings point to the potential use and effectiveness of internet interventions in the management of quality of life in AS patients.

Interestingly, the results produced by Kazer et al., (2011) are mirrored extremely closely by those of Osei et al., (2013) who very recently assessed the use of a 6-week online intervention on quality of life and treatment side effects in radically treated PCa patients. The internet intervention compromised of an online support forum where PCa patients could interact with

each other whilst providing information about treatment side effects, managing side effects and PCa information. No specific relaxation or stress management information was provided.

The results indicated that in comparison to the control group, PCa patients undertaking the online intervention saw significant improvements in quality of life, with the greatest gains observed in urinary function, sexual health and hormonal health. However, as was observed by Kazer et al., (2011) these positive alterations to quality of life were not maintained at follow up. This again suggests that the significant benefits observed in PCa patients undertaking online interventions are relatively transient.

However, the findings generated by both Kazer et al., (2011) and Osei et al., (2013) suggest that online interventions are effective, at least over the short term, at improving the quality of life of PCa patients. Additional long term support in the form of prompting emails, telephone calls, text messaging and mobile apps may help to maintain these short term transient benefits into deep seated and more permanent ones (Kazer et al., 2011). If this were the case then online interventions may offer a novel, fruitful and cost effective means of equipping PCa patients with the resources needed to improve psychological health and wellbeing.

But if internet interventions such as Alive and Well which have been designed specifically for AS patients are to be investigated, it is fundamental that clinically relevant dependant variables are utilised. Whilst assessing the impact and effectiveness of interventions such as Alive and Well on quality of life is important, it is crucial that measures of anxiety also be recorded. AS patients who are anxious are significantly more likely to transfer to clinically unnecessary radical intervention (Latini et al., 2007; Patel et al., 2004). Because of this, managing anxiety in AS patients has been identified as an area of urgent address and focus in the related literature (Pickles et al., 2007). If internet interventions such as Alive and Well are found to be effective at reducing anxiety in the same way as they have been for improving quality of life, they may offer a clinically effective and economically sustainable means of lowering the number of AS patients transferring to unnecessary radical treatment. Additional longitudinal research utilising valid and reliable measures of anxiety would be beneficial to address this issue.

5.4.4. Self-care interventions that were delivered by any other means

To date, only one investigation has utilised a one-to-one support intervention among men with PCa. In their investigation, Weber et al., (2003) randomised 30 post-radical prostatectomy patients to either a control group or an experimental group. The former received routine care. The latter were paired up with long-term survivors of PCa who had undergone radical prostatectomy themselves over 5 years previously and shared similar treatment side effects. Participants and the long-term survivors met once a week for 8-weeks. The rationale for this intervention was the male cancer patients have poor recruitment and adherence rates to group interventions and thus dyadic support may offer a more appealing option.

The results revealed that men in the experimental group reported significantly lower levels of depression and significantly higher levels of self-efficacy in comparison to men in the control group. Furthermore, all men randomised into the experimental group attended all 8 sessions. These results suggest that dyadic support interventions that are offered by lay support partners who have themselves lived through a PCa diagnosis, treatment and the accompanying side effects offers an effective means of improving psychological health in post-treatment PCa patients. Given the reduced costs associated with lay peer support in comparison to health-care practitioner delivered interventions, developing interventions that are delivered to PCa patients through trained lay support partners may offer a potentially fruitful avenue of research.

Unfortunately, no other investigations have adopted this approach which means that it is currently not possible to determine whether these results would be replicated. Furthermore, dyadic interventions of this nature pose numerous logistical problems which would make them hard to integrate into routine care. This limits the practical applicability of such approaches. For example, where should the dyad meet? If in private homes who would safeguard and insure the patient and lay supporter? If in a clinical setting, dyadic interventions become less manageable as only one patient can be supported at a time compared to the 10-15 who could be supported in a group setting. Lastly, whilst there appears to be a large volume of PCa patients requiring support (Chambers et al., 2011), there may be less so who are willing to offer it and become lay support partners. If insufficient numbers of the latter exist, then a dyadic intervention of this nature would very quickly become impractical to deliver. Whilst this approach provided both a novel and effective form of psychological support, the problems

posed by trying to transfer it to routine care means that it is unlikely to develop into a sustainable form of support for PCa patients.

5.5. Discussion

The aim of this literature review was to determine the extent of the evidence base into the use of self-care interventions within the field of PCa. It has shown that a small, heterogeneous and quickly growing foundation of evidence currently exists which has utilised many interesting and novel self-care approaches to help PCa patients better manage the psychological distress of being diagnosed with, treated for and surviving from PCa.

Furthermore, it was encouraging that I was able to identify several investigations that have utilised group based support interventions as a means of addressing psychological functioning among AS patients. As it was my intention to trial a group based MBSR intervention in a sample of PCa patients in this PhD, it was important to ascertain whether the previous research had been able to effectively recruit patients into group interventions.

From the available evidence it would seem that group based interventions are well received by PCa patients with evidence of good recruitment and adherence in both short and long term interventions. Indeed, even in group support interventions that required large time commitments from the patients (10-weeks and over 20 hours of group contact time), substantial numbers of PCa patients were sufficiently interested in the intervention to recruit and adhere to it (Penedo et al., 2004). Whilst the 10-week intervention designed by Penedo was not offering MBSR, it would still suggest that the time demands of the 8-week MBSR intervention I hoped to pilot would not be a barrier to recruitment.

However, throughout the running and interpretation of this narrative review, it was important for me to be aware of my own motivations and biases and the ways in which these may have impacted upon the generated findings. For example, as a PhD project, it was necessary for me to have devised and planned a structured package of work that would allow me to successfully fulfil the obligations of a thesis submission. Therefore before this review was conducted, it was already my aim and intention to run an 8-week MBSR intervention among a sample of AS patients. The time demands of applying for and securing ethics and R&D approval and all of

the required sponsorship and insurances meant that the decision to run this study had been confirmed prior to this review. There was therefore the risk that I was selectively choosing studies that supported and validated my intention to trial an 8-week MBSR intervention rather than providing an informed and objective account of the use of self-care interventions within the field of PCa.

Through personal retrospective reflection I can see that I was in certain instances using the review process to provide a rational for, and further support my pre-conceived intention to deliver, an MBSR intervention. This represents an important limitation to this review and one that needs to be taken into account when interpreting the generated findings.

However, despite this, I do feel that the current review supported and provided an objective rationale for delivering a mindfulness based intervention to a sample of PCa patients based upon the weight of evidence suggesting that PCa patients are willing to recruit into and adhere to long term (10-week) group based stress management interventions. This was aided by the systematic search protocol utilised which reduced the likelihood of identifying, selecting and discussing articles which specifically supported my decision to utilise a MBSR intervention, such as the work conducted by Penedo et al., (2004), at the expense of those that didn't.

It was also an aim of this study to determine whether any previous investigations have utilised mindfulness based interventions in men with PCa. Only one longitudinal investigation did so (Carlson et al., 2003; Carlson et al., 2007) but they recruited mixed cancer populations of which the PCa patients made up only a small percentage and no data relating to the PCa patients as a specific sub-set was presented. Whilst it was therefore unfortunate that no investigations were identified that utilised mindfulness based techniques specifically within a sample of PCa patients, several of the investigations overviewed in this review used breath based relaxation training and stress management techniques (Parker et al, 2009, Penedo et al., 2004; Carlson et al., 2003). Insufficient detail about these techniques was provided by the authors to allow me to determine how closely they mirrored those offered under the standard syllabus of MBSR. However, it was encouraging that these investigations were able to successfully recruit substantial numbers of PCa patients into interventions that utilised breathing based exercises to help combat stress, anxiety and uncertainty and improve functional quality of life.

A strong view prevails within the sociological research of the importance that male cancer patients place on maintaining a stoic acceptance of their diagnosis and prognosis and on not admitting to feelings of concern or distress (Moynihan, 2002). During a health related crisis men feel under great pressure to maintain this society induced gender stereotype even if privately they wish for additional help and support (Moynihan, 1998; Moynihan, 2002). It has been postulated that self-care interventions that aim to teach PCa patients relaxation techniques are likely to be largely ineffective as recruitment into such interventions would firstly require the patient to openly admit that he is experiencing distress and requires help and support. However, the findings from this review would suggest that this is not the case and that PCa patients are willing to recruit into and adhere to self-care interventions that provide them with techniques to self-manage any psychological distress they are experiencing. This may suggest that the mindfulness techniques that I plan to offer to AS patients within this PhD may be well received.

It is interesting that all of the group interventions identified in this review utilised general quality of life as their primary dependant measure. Only two (Parker, 2009; Burglund et al., 2007) specifically assessed depression and none anxiety. As has been discussed, anxiety is an extremely important condition within PCa, particularly for patients being managed with AS. Quality of life is a heterogeneous psychological construct that contains components of myriad conditions such as mood, uncertainty, stress, fear and depression. There is little evidence or rationale to support the notion that just because the group interventions overviewed in this review were largely effective at improving quality of life, they would be equally effective at targeting anxiety. This represents a distinct void in our understanding of how to manage unique psychological conditions such as anxiety and depression within PCa patients. To address this issue it is fundamental that future research aims to assess the effectiveness of group support as a tool to target specific psychological constructs such as anxiety. Doing so would allow for the generation of a working model into how the specific psychological mechanisms of group support may help PCa patients to better manage conditions such as anxiety and depression.

Likewise, none of the group interventions overviewed in this review specifically targeted AS patients. It is unlikely that group based self-care interventions that are designed specifically for the requirements of men treated radically will also be effective at managing the psychological needs of men being passively managed with AS. The increasing utilisation of AS in the UK and

the long survival rates associated with men being managed this way means that developing self-care interventions specifically for this patient cohort should be viewed as an issue of critical importance.

This review has also highlighted several group interventions that have focused primarily on information provision as a means of combatting psychological distress by improving patient health literacy. The results of these investigations were mixed with some showing effectiveness with very brief group interventions whilst other longer interventions were largely ineffective. These inconsistencies were likely due to methodological faults rather than the inherent nature of the interventions. As self-care interventions that utilise information provision as a means of improving psychological health have shown promising results in other cancer sites (Kissane et al., 2007; Guo et al., 2013; Cimprich et al., 2005), further research would be beneficial to determine more conclusively whether such an approach would prove effective within the realms of PCa. This may be particularly true for men being managed with AS.

In conclusion, this review has highlighted that self-care interventions within the field of PCa offer a degree of effectiveness at improving the psychological health and wellbeing of this patient group. More specifically, several investigations exist to support the use of group based support for men with PCa. The recruitment and adherence rates and the clinical effectiveness observed in these group interventions are encouraging and suggest that the widely held assumption that older male cancer patients are inherently disinclined to recruit into group support is largely unfounded. Furthermore, several of these group interventions were long in duration and offered breathing based stress management techniques. As one of the primary aims of this review was to determine from the available evidence the likelihood of being able to successfully recruit a sample of PCa patients being managed with AS into a MBSR breathing based self-care intervention, these findings are encouraging and suggest that MBSR may offer an acceptable form of support that AS patients will be willing to recruit into and adhere to.

Chapter 6

A Feasibility and Qualitative Evaluation of Mindfulness Based Stress Reduction in the Management of Depression and Anxiety in Prostate Cancer Patients being Managed with Active Surveillance.

6.1. Research Question: Does Mindfulness Based Stress Reduction offer a feasible and effective intervention for the management of depression and anxiety in PCa patients being managed with AS?

Primary Feasibility Objectives

- Determine the ability to recruit AS patients into the MBSR trial
- Determine whether the clinical care team were willing to recruit/be involved in the recruitment process
- Assess patient adherence to the intervention
- Assess patients willingness to be interviewed three times
- Assess patients willingness to complete the questionnaires
- Determine whether patients found the questionnaires acceptable

Secondary Objectives: Qualitative

- Provide a novel insight into the beliefs, meanings and experiences of AS patients using MBSR in the management of depression and anxiety.
- Determine the ways in which the standard MBSR program could be modified or adapted to allow it to be better suited for, thus making it more appealing to, AS patients.
- Allow for the better understand of the active psychological mechanisms of MBSR.

Secondary Objectives: Quantitative

- Determine the effect of a standard MBSR intervention on changing depression and anxiety scores over a 4 month period (8 week intervention and 8 week follow up).
- Determine the effect of a standard MBSR intervention on changing stress and coping scores over a 4 month period (8 week intervention and 8 week follow up).
- Determine the effect of a standard MBSR intervention on patient levels of mindfulness over a 4 month period (8 week intervention and 8 week follow up).

- Collect data that will allow for the powering and design of a larger randomised controlled trial (RCT) should the data suggest effectiveness.

6.2. Introduction

The receipt of a positive cancer diagnosis is generally interpreted as a life threatening event and as such has been shown to induce substantial and often prolonged impairments to psychological and emotional health. Such impairments typically include depression, anxiety, fatigue, reduced quality of life and insomnia (Brown & Kroenke, 2009; Cheng & Lee, 2009; Pasquini & Biondi, 2007).

These conditions are undesirable and go on to negatively impact upon the clinical management of cancer through inducing lower patient treatment compliance, an increased number of missed outpatient appointments, higher rates of hospitalisation, poorer medical decision making, increased utilisation of medical resources and ultimately a reduction in overall patient quality of life (DiMattoe et al, 2000; McDaniel et al, 1995 ; Smith, Gomm & Dickens, 2003; Pirl et al., 2002 Watson et al, 1999). Interventional support that allows conditions such as depression and anxiety to be better and more effectively managed are thus required.

In recent years, the better management of the psychological and emotional needs of cancer patients across the trajectory of the cancer journey has become an issue of increased importance within the national framework for cancer management within the UK (Department of Health, 2011). This is primarily because cancers are being diagnosed earlier and patients are living longer (Office for National Statistics, 2011). Consequently the management of survivorship agendas has developed into a key research priority (Department of Health, 2011).

This is best highlighted by the creation and implementation of the National Cancer Survivorship Initiative (NCSI). The NCSI strives for the more holistic management of cancer with the aim of affording patients the support they need to live full, enjoyable and active lives throughout their cancer experience (National Cancer Survivorship, 2010). Furthermore, the current consensus stipulated by the Department of Health recommends that psychological interventions form a fundamental component of this whole person approach to cancer survivorship (Department of Health, 2006).

One such psychological intervention that has shown promising early results as a tool to allow cancer patients to better manage the psychological and emotional side effects of cancer diagnosis, treatment and survival is Mindfulness Based Stress Reduction (MBSR).

MBSR is a psycho-educational support programme, created in the meditative traditions of Buddhism, which aims to empower patients to experience life in a non-judgemental and transient way (Kabat Zin, 1990). MBSR emphasises the importance of accepting all thoughts and experiences as they are, good and bad alike, without trying to alter or change them. In doing so, one learns to live more readily in the present moment (i.e. more mindfully), which in turns allows one to prevent the constant ruminative processes of what may happen in the future.

Through living in such a way, one also learns to accept the transient and impermanent nature of negative experiences and that just because something "currently is", does not mean it will "always be" that way. It is posited that in this way patients build up a greater tolerance to, and acceptance of, negative, unwanted and painful experiences. This in turn allows them to reframe their experiences more positively when managing a cancer diagnosis, leading to reduced psychological distress (Shapiro et al., 2003; Carlson et al., 2003, Carlson et al., 2007; Carlson & Garland, 2005).

6.2.1. MBSR in the management of psychological morbidity in cancer care

Current evidence has observed that cancer patients undertaking mindfulness training experience reductions in depression, anxiety, stress and general mood disturbance, and increases in quality of life and general wellbeing (Carlson et al., 2003; Carlson et al., 2007; Garland et al., 2007; Wite-Janusek et al., 2008; Lengacher et al., 2010; Speca et al., 2000).

For example, in a recently conducted trial, Lengacher et al., (2010) randomly assigned 84 female breast cancer patients to receive a standardised 8-week MBSR programme versus usual care whilst measuring a battery of psychological and emotional states. The results indicated that after the completion of the programme, the patients assigned to the mindfulness group experienced significantly lower scores for depression and state and trait anxiety and enhanced overall quality of life in comparison to the control group.

Similarly, an often cited study conducted by Speca et al. (2000) assessed the effectiveness of MBSR in the management of mood disturbance and stress in a randomly selected sample of cancer patients. The results highlighted that the patients undertaking the mindfulness training experienced a 65% reduction in total mood disturbance, depression, anxiety and anger incidence. They also observed a 35% reduction in overall stress levels.

Crucially, the benefits observed by Speca et al., (2000) were maintained when the same patients were re-assessed six months later (Carlson et al. 2001). Such findings were the first of their kind to highlight not only the psychological benefits of mindfulness training in cancer patients but also the durability and longevity associated with them.

Over the last decade, several well conducted systematic reviews and meta-analyses into the application of MBSR in the management of psychological distress in cancer care have been published (Shennan, Payne & Fenlon, 2010; Ledesma & Kumaon, 2009; Musial et al., 2011), a sure sign of the rapidly developing volume of research within this area.

6.2.2. What is the evidence for the use of MBSR in male cancer patients?

The most recently conducted systematic review of mindfulness based interventions in cancer care (Musial et al., 2011) highlighted only four individual investigations that included male cancer patients among those recruited (Carlson et al., 2003; Carlson et al., 2007; Birnie, Carlson & Garland, 2010; Garland et al., 2007). In all cases these patients were recruited as part of a larger, mixed sample of cancer patients that were comprised predominantly of female breast and ovarian cancer patients. Across these four studies, the number of male patients recruited totalled forty three. This is in stark contrast to the 296 breast cancer patients identified by the same review and recruited across twelve independent studies.

Unfortunately, there was no stratification of the data by gender in the four studies that recruited male cancer patients. Consequently it was not possible to ascertain how effective the mindfulness interventions were at impacting upon psychological health for the male patients. Given that in all four studies the number of male patients recruited was substantially less than their female counterparts, it is possible that the significance observed in the findings relating to enhanced psychological wellbeing may have related to the preponderance of female patients recruited; similar findings may not have been mirrored in the smaller proportion of male patients included within these studies.

To date we currently have very little understanding of the uptake, adherence and effectiveness of mindfulness based interventions within male cancer populations and research specifically assessing the effectiveness of MBSR in an exclusively male cancer population has yet to be undertaken. A concerted research effort is needed to address this issue. A particularly fruitful avenue for such research may exist within the realms of prostate cancer (PCa).

6.2.3. MBSR, prostate cancer and active surveillance

Survival rates for men diagnosed with PCa are very good, with over 60% of those diagnosed living for ten years or more (Office for National Statistics, 2007). However, living with cancer for such a substantial period of time is challenging, especially within a population of older males.

For PCa patients being managed with AS, such survivorship issues may be further accentuated by the unique nature of their treatment. The use of AS for clinically suitable men is increasing in the UK as we diagnose PCa earlier and increasingly understand the 'balance' of benefits versus risks involved with a more aggressive approach to management. In light of this, the development and assessment of economically viable self-help techniques that allow AS patients to self-manage their psychological distress over the long-term, and to live and mange well whilst part of an AS cohort, are of paramount importance within the survivorship agenda.

MBSR has never been applied and assessed specifically within a group of PCa patients. Yet due to the underpinning values of mindfulness, it could prove to be an effective approach for this patient group. This may be particularly true for PCa patients being managed with AS. The core concept of mindfulness is in allowing an individual to live in the present moment, in the "here and now", rather than ruminating or catastophising about the future (Kabat-Zinn, 1990). Though doing so the individual is able to learn to observe their thoughts in a non-judgemental way and realise that their thoughts are not facts, but rather their mind ruminating about what may happen, instead of what actually is happening. By acknowledging the present moment in this way, one is able to reduce the psychological burden they are experiencing due to ruminations and preoccupations with the future which results in lower levels of anxiety, stress and depression (Shapiro et al., 2006).

Research suggests that the psychological and emotional problems experienced by men on AS stem from their fears that their disease isn't being radically treated and may be progressing unchecked (Hedestig, Sandman & Widmark, 2003). Clinically this is highly unlikely as the structured monitoring process central to the use of AS, which involves regular PSA checks, imaging and biopsies, ensures that unchecked progression is highly unlikely.

Through practising mindfulness, AS patients may be able to ground themselves in the present moment and acknowledge that all of their clinical markers suggest a stable, non-aggressive and non-progressive cancer. Through cultivating a state of present moment mindfulness in this way they may be able to non-judgementally acknowledge that the majority of the fears and

anxieties they harbour are a result of their ruminative thoughts and catastrophisation and not objective clinical facts. In this way, they may be able to live in the present moment with more awareness and in doing so reduce the levels of anxiety and depression they are experiencing.

In addition to this theoretical support for the use of MBSR as a means of managing distress among a sample of AS patients, I also obtained considerable Public Patient Involvement (PPI) input which consistently suggested that MBSR may offer a suitable and effective form of support for this patient group.

Firstly, during the initial design of this investigation I made contact with and regularly spoke to an expert patient representative of the Prostate Cancer Charity (recently rebranded as Prostate Cancer UK). Over a period of several months I conducted several telephone meetings with the patient representative and outlined the aims, objectives and methodology of the planned MBSR study. I received considerable input and advice from these conversations (such as reducing the session length from the standard 2.5 hours to 2 hours) and the overriding view of the patient representative was that an intervention of this nature would be appealing to and would likely address the key concerns and fears of AS patients.

Secondly, the patient representative was an active committee member of PCaSO which is a large local PCa support charity. In this capacity the patient representative introduced me to the chairman of PCaSO who was instrumental in allowing us to identify a sample of AS patients who were able to subsequently input into and review the methodology of the study. This second round of PPI again suggested that an 8-week MBSR intervention of this nature was well received by a small sample of AS patients who collectively stated that if offered to them they would have opted for and recruited into the trial.

Despite the robust theoretical rationale for utilising an MBSR intervention in this patient group and the considerable PPI input obtained, a foundation of sociological research exists to highlight PCa patients' inherent aversion to support groups that address emotional and psychological concerns (Chapple & Ziebland, 2002). Consequently involving and recruiting AS patients into a MBSR programme may be difficult. MBSR may not be as effective at positively modulating depression and anxiety for patients with PCa as it has been for breast cancer. Will PCa patients accept MBSR and find it useful and if so in what ways? What are their likely adherence rates and in what ways may we be able to modify the standard 8-week programme to address and optimise these issues?

The aim of the current investigation was to address these issues and conduct a mixed methods exploratory study into the effectiveness of MBSR in the management of depression and anxiety in PCa patients being managed with AS.

The use of in-depth interviews will provide a unique insight into the workings of MBSR within this population, helping me to understand the psychologically active mechanisms of MBSR for future studies (if relevant). Secondary quantitative analyses of changing depression and anxiety scores will allow me to determine the specific clinical impact of the mindfulness intervention upon psychological distress and power a more definitive pragmatic trial, should that be indicated.

6.3. Method

6.3.1. Recruitment Procedures

Patients will be approached for recruitment from the prostate cancer clinic at Southampton General Hospital under the guidance and supervision of Mr Brian Birch, Principle Investigator and lead consultant urologist.

Full ethical approval for this study was granted by the Oxfordshire Research Ethics Committee on 3rd April 2012 (REC: 11/SC/0035; see Appendix 10). Sponsorship and the necessary insurance requirements were provided by the University of Southampton (Appendix 11).

Patients will initially be identified through the screening of the patient records at the prostate cancer clinic to identify suitable patients who qualify for inclusion into the study based on the pre-determined inclusion and exclusion criteria (see below).

Once the records have been screened, a full list of eligible patients will be drawn up. Each patient will then be sent, by post, a Patient Information Pack (PIP) directly from the clinic which will include:

I. Patient Invitation Letter (PIL) – The PIL will provide the participant with a brief overview of the investigation and will inform them of what to do next should they wish to take part.

II. Patient Information Sheet (PIS) - The PIS will provide a detailed introduction and overview of the intervention, informing each participant of what their involvement would entail should they decide to take part, who will be conducting the research, their rights as participants and who to contact for more information

III. Patient Reply Slip (PRS) – The PRS will provide the participant with a means of informing the research team that they would, or would not, like to hear more about the investigation.

IV. A Freepost return envelope – This will be included within the PIP to allow the participants to return the PRS to the research team at Aldermoor Health Centre

All of the documents included in the PIP can be seen in Appendix 12.

Once the PIP's have been mailed out, I plan to wait for one week before identifying all non-responders. Each non-responder will then be contacted once, by telephone, to enquire into whether or not they would like to take part in the study. If they do, they will be asked to return the PRS as per the instructions listed in the PIL, if they still had it. If they didn't the patient will be re-sent a PIP to ensure they have a copy of the relevant information and they will be asked to re-read this and then send in the PRS if they still wished to partake in the study. Completing and sending in the PRS will indicate initial consent for the patient to be contacted by telephone to have the study described in greater detail and to answer any questions the patient may have.

Once all the PRS have been received, each patient will be contacted and given a detailed verbal overview of the study by telephone. The purpose of this will be to answer any questions the patient may have had and to ensure that before consenting to partake in the study, the patient is fully informed of the time demands of the study and the procedures they would be undertaking as part of the investigation.

The telephone call will also allow me to assess the suitability of the patient to undertake the MBSR programme and to ensure that the patient was fully committed to attending the 8-week MBSR programme and completing the required homework (section 4), be interviewed three times over the duration of the study (section 5) and complete a series of brief questionnaires (section 6). This will ensure that all participants are fully informed about the commitment required of them.

Patients who are willing to undertake the programme and were deemed suitable to do so will be sent a written informed consent form to read, sign and return (Appendix 12).

Upon receipt of the signed consent form, the patient will be deemed to be officially recruited into the study. Each patient will then be provided, by post, with the dates, times and location (with maps) of the MBSR group they would be attending. Each patient will also be contacted to

arrange the dates and times of their three interviews which were to be conducted prior to, and the end of and 2-months after the completion of the 8-week programme (see section 6.3.3).

Sample

It was my aim to recruit 30 men into the current investigation, all of whom must have fulfilled each of the following criteria:

Inclusion and Exclusion Criteria

I. A biopsy confirmed diagnosis of PCa.

II. Undergoing AS as their primary treatment option.

III. No previous radical treatment for PCa.

IV. Diagnosed over two months previously to avoid the acute mood disturbances associated with the initial shock of diagnosis.

V. Have no additional cancer diagnoses or other serious life threatening comorbidity.

VI. Fluent in the English language.

VII. Provided informed written consent.

6.3.2. MBSR Intervention

Study Duration

The study duration for each participant will be 4 months; a 2-month MBSR course and 2-months follow up thereafter.

MBSR Intervention

Participants will take part in eight 2-hour weekly sessions run over an 8-week period in keeping with the standardised programme created by Dr. Kabat Zinn (1990). Such a design has been shown to optimise patient benefits whilst being as minimally intrusive, time wise, as possible. Each weekly session varies but all will involve the common core practices of; the Body Scan, Guided Sitting Meditation, Mindful Stretching and Mindful Walking.

Home Practice

Home practice represents a crucial component of the MBSR process. Participants will b taught how to bring mindfulness into their everyday lives and a series of CD's will support the daily practice which will involve a suggested 30 minutes per day. The CD's will provide a flexible range of guided meditations (some as short as 10 minutes to acknowledge the different needs and preferences of individual participants).

Half Day Mindfulness Session

All participants will also be asked to complete one 4-hour day of mindfulness in week 6 (in addition to the 2-hour session) to help embed the self-management techniques into the participants' daily lives and to help resolve any difficulties they may be experiencing.

Mindfulness Instructor

Mr Philip Russell is a fully qualified and experienced nurse, counsellor and mindfulness instructor who currently works full time at the Rowans Cancer Hospice providing mindfulness and counselling services to their cancer patients. It is important that I understand the instructor's personal reflections on the mindfulness process and to assist with this Mr Russell will be asked to keep a reflective diary of the processes involved.

6.3.3. Qualitative Study

All participants taking part in the MBSR course will be invited to undertake 3 qualitative interviews; one prior to the MBSR course, one at the end of the course and one 2-months after the completion of the course. Each round of interviews will be constructed to allow me to elicit key information relating to the patients understanding of their illness, their treatment and MBSR:

Interview 1: (Pre-MBSR)

In depth interviews will be conducted with a series of "grand tour" questions (Spradley, 1979). These will be used to elicit contextual insights into each participant's individual cancer experience. Tailored semi-structured questions will be utilised to ascertain relevant information regarding the patients views on being treated with AS and the impact this has had upon their lives, the motivation underpinning their reasons for selecting AS, their views on the MBSR programme and what they hoped to achieve through taking part in the study.

Interview 2: (Post-MBSR)

Semi-structured interviews will be conducted to explore the participants' subjective views, beliefs and understandings of mindfulness and to determine how mindfulness changed or impacted upon their daily lives. The interviews will aim to further elicit the benefits and disadvantages of mindfulness and assess how it helped or hindered in the management of any depression and anxiety. They will also explore the areas and components of the programme that the patients found most useful and the ones they found to be less useful. I will also ask the patients for their generic views and comments on the ways in which the 8-week programme could be modified and/or adapted to make it more appealing to PCa patients.

Interview 3: (2-Months Post MBSR)

Semi-structured interviews will again be conducted to allow me to better understand the participants continued understanding of mindfulness and to determine whether mindfulness still continued to be a part of their daily life and if so, why.

6.3.4. Qualitative Data Analysis

Analysis of qualitative data will be inductive and will draw upon the thematic analysis approach to data analysis (Braun & Clarke, 2006; Silverman, 2011). Repeated readings of the interview transcripts will allow for the identification of important themes. Standard procedures to ensure rigour will be used (negative case analysis, double coding, clear definitions of codes, informal respondent validation and detailing a clear audit trail). A detailed and comprehensive overview of the qualitative methodology I would have used in this investigation can be seen in Chapter 7 (pages 158-170).

Analysis of the data in this way would have provided novel insights into the common beliefs, meanings and experiences of the role of MBSR in the management of depression and anxiety among AS patients. The analysis would also allow me to better understand the patients' subjective beliefs about MBSR and the ways in which the standard program could be modified or adapted to allow it to be better suited for, thus making it more appealing to, PCa patients.

6.3.5. Quantitative Feasibility Study

Whilst primarily a qualitative study, the current investigation also utilised a series of quantitative measures to assess a variety of psychological states.

Primary Outcome

The primary quantitative outcome of this study was depression and anxiety scores as assessed at baseline and monthly for 4 months. This would allow me to reach one of my predefined research objectives of determining the effectiveness of MBSR at managing depression and anxiety.

Depression and anxiety was measured by the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983). The HADS is an extremely well validated and reliable questionnaire that has been used extensively within the field of oncology to assess the prevalence of depression and anxiety among cancer patients. A full assessment and overview of the validity and reliability of the HADS has already been provided in Chapter 4 of this thesis (section 2.2.4).

Briefly, the HADS is a 14-item scale specifically designed for patients with medical illnesses and it excludes somatic items and relies only on emotional symptoms of depression and anxiety. Seven questions relate to symptoms of depression and seven to anxiety as experienced over the previous week, using a Likert scale. The maximum score is 21 on both the anxiety and depression subscales. A HADS score of ≥8 indicates borderline levels of depression and anxiety whilst scores of greater than 11 are indicative of clinical levels of depression or anxiety. For the current investigation, depression and anxiety was deemed to exist in patients with a HADS score of ≥8. Additionally, the largest previously conducted investigation into depression and anxiety prevalence in PCa patients undergoing AS also utilised the HADS (Burnet et al., 2007), making the results obtaining through the current investigation directly comparable to those reported by Burnet et al., (2007).

Secondary Outcome

1. Stress and Coping (baseline and monthly for 4 months)

The COPE questionnaire is a multidimensional scale that was devised to gauge the way individuals respond to stress (Carver, Scheier & Weintraub, 1989). It has repeatedly demonstrated high levels of internal validity and has been used extensively within oncological care to measure and monitor patient coping strategies (Lyne & Rogers, 2003). This outcome measure was selected to allow me to reach one of my predefined research objectives of determining the impact of the MBSR intervention on stress and coping ability.

2. Mindfulness (baseline and monthly for 4 months)

The Toronto Mindfulness Scale (TMS) was constructed by a consensus group of experienced mindfulness practitioners and researchers involved in cancer research to operationalise Shapiro's model (Shapiro et al., 2006) of mindfulness (Lau et al., 2006). Internal validity, factor constructs (curiosity & decentring) and criterion validity was evaluated in a study of 400 people to derive a 15 item, 2 factor questionnaire (Lau et al., 2006). It was further evaluated among 99 participants in an 8-week MBSR programme with a range of conditions, including chronic pain, diabetes and multiple sclerosis. This outcome measure was selected to allow me to reach one of my predefined research objectives of determining the impact of a standard MBSR intervention on patients perceived levels of mindfulness.

6.3.6. Quantitative Data Analysis

Descriptive statistics will be performed on the HADS, COPE and TMS scores to determine changes over time. Correlation and regression analyses will then be run to assess any relationships between changing HADS and changing mindfulness scores, as assessed by the TMS. It was hypothesised that reductions in HADS would correlate significantly to an increase in TMS scores, suggesting that mindfulness acts to increase psychological health and wellbeing in AS patients.

I also planned to use the HADS data to help power and design a larger randomised controlled trial (RCT) should the data suggest efficacy. More specifically, previous research suggests that a change of 3 units on the HADS scale represents a clinically significant improvement in depression and anxiety (Cameron et al., 2008). Power calculations suggest that a single sample of 30 patients would be sufficient to have a 90% power to detect a statistically significant change of 3 units in the HADS from baseline to end of treatment. Thus an initial pilot/feasibility study of this nature, utilising 30 participants, would provide valuable data to facilitate the estimation of sample size for the design of a larger RCT in the future.

6.4 Results

At the time of recruitment, clinic records at the PCa clinic at Southampton University Hospitals Trust revealed that there were 46 men with localised PCa who were being managed with AS. All 46 of these patients were contacted and invited to partake in the current investigation. By contacting all of the patients in this way I hoped to minimise any form of selection bias and thus increase the representativeness of my sample.

Of the 46 Patient Invitation Packs sent out, 6 patients returned the Patient Reply Slip to indicate that they did not wish to take part in the study. Only two of these 6 patients provided an explanation as to why, which in both cases was that the time commitment required was too demanding.

Of the 40 non-responders, I was able to successfully contact 39 by telephone within 1 week of sending out the original Patient Invitation Packs. I was unable to make contact with one patient despite numerous calls and messages. Full permission to contact non-responders by telephone in this way was granted by Oxfordshire REC as part of the follow up recruitment protocol.

Each patient was subsequently asked if they had received the Patient Invitation Pack and if so whether they would like to take part in the study. In all cases the men were spontaneously willing to discuss the study in more detail.

When asked to discuss why they did not wish to enter the study I established that 2 of the men wanted to take part in the MBSR trial. The first worked twelve hour shift work and was thus unable to commit to the 8-week course. The second also wanted to take part but was due to initiate radical treatment (prostatectomy) that month and would thus no longer fulfil the inclusion criteria of being treated with AS.

All of the remaining 37 patients stated that they did not wish to take part. Their reasons for this fell into one of 5 general categories (N.B. the number of patients stating each reason is listed in brackets)

1. The time commitment was too demanding (n=19).
2. They had too far to travel (n=6).
3. They didn't like the concept of MBSR (n=3).
4. They weren't suffering from depression, anxiety or distress (n=5).
5. No reason given (n=4).

As part of the ethics application process, Oxfordshire REC had granted me permission to record this data (i.e. the reasons why non-responders had decided to not take part in the study) but only anonymously in hard copy format; the use of audio recording devices to record the follow up telephone conversation was not permitted. I was also not permitted to interview the men during the follow up telephone call but the REC fully accepted that the follow up would entail a degree of conversation, questions and answers which they deemed acceptable.

Therefore over the course of the telephone conversation I was provided with a clear justification from each non-responder as to why they did not want to take part in the study and a variety of other issues they decided to bring up during the course of the telephone call. This information I recorded anonymously in hard copy format in a note book. A key pattern that emerged from these telephone conversations was the degree of psychological distress and anxiety these men were experiencing. Of the 37 AS patients that I spoke to over the course of these follow up conversations, 30 (81%) made a direct reference to the fact that they were experiencing a meaningful level of distress and anxiety. Furthermore, 26 of the 37 patients made a direct reference to the fact that they felt there was a distinct lack of information, education and support around their diagnosis and subsequent treatment with AS.

Whilst these results lack methodological rigour due to the restraints imposed by the Oxfordshire REC (i.e. not being able to record the telephone conversations or conduct interviews with them during the follow up), they still provide an important insight into the problems and supportive needs of these AS patients.

6.5. Discussion

6.5.1. Overview of Results

The aim of the current investigation was to assess the feasibility and effectiveness of a standardised MBSR intervention as a tool to manage depression and anxiety in a sample of PCa patients being managed with AS. To the best of my knowledge, this investigation was the first of its kind to do so.

The key finding of the current study was that men diagnosed with PCa who were being managed with AS were disinterested in, and unwilling to recruit into, a standardised MBSR programme that was being offered as a tool to allow them to better manage psychological distress.

6.5.2. Limitations of the Research

Prior to the current investigation, MBSR has never been offered to and trialled within an exclusive sample of PCa patients. Thus the current findings suggest that in its standardised 8-week format, MBSR does not represent an acceptable intervention to men with slow growing localised PCa who are being managed with AS.

A key limitation of the current investigation was the assumption that MBSR would be viewed as acceptable to these men without adequate preliminary evidence to suggest that this would be the case.

Given the large foundation of research attesting to the willingness of female cancer patients to recruit into mindfulness based interventions (Musial et al., 2011), and the contrasting lack of uptake into such interventions observed within the literature by their male counterparts, it is probable that gender stereotypes may play a central role in understanding the male populations disinterest and possible distrust in mindfulness based interventions.

Gender, and the concept of masculinity, represents an issue of considerable influence when determining the ways in which male cancer patients respond to and manage both their diagnosis and their treatment (Oliffe & Thorne, 2007; Moynihan, 1998). Research suggests that the ways in which men play out and maintain their gender roles when facing a life threatening illness are both consciously and subconsciously impacted upon by the culture and society they operate in (Moynihan, 1998; Moynihan, 2002, Oliffe & Thorne, 2007).

The stereotypical cultural characteristics of masculinity are defined by a variety of core values such as the restricted experience and expression of emotion, toughness, self-sufficiency, stoicism and the maintenance of a "suffering in silence" attitude (Moynihan, 1998). Men go to great lengths to maintain and protect their gender role when facing a health crisis (Moynihan, 1998; Moynihan, 2002). It has been suggested that when facing a PCa diagnosis, men face a culturally induced pressure to cope, adjust, move on and accept their condition, and the impact that the condition has had upon their lives, with an outward façade of stoicism (Oliffe & Thorne, 2007).

The evidence would suggest that AS patients experience relatively high prevalence of depression and anxiety (Burnet et al., 2007). Indeed, recent research compiled as part of this PhD observed depression and anxiety in men being managed with AS to be as high as 12% and 23% respectively. Such data are almost three times that experienced by the over 65's in the UK (Department of Health, 2011) and equal to those typically observed by female breast cancer patients (Pasquini & Biondi, 2007).

It is possible that many of the men approached for recruitment into the study may have been experiencing a degree of distress. Indeed, 81% of the men I spoke to over the telephone during the recruitment process made specific reference to the fact that they were experiencing a substantial degree of psychological distress. These patients may have wanted to take part in

the offered MBSR trial but feared that through doing so they would risk exposing their need for support and thus break their conformity to their masculine identity.

A second key limitation of the current investigation was the failure to screen potential patients as a function of time since diagnosis. To be deemed suitable for management with AS, the patient's clinical markers must all exist within a set range of parameters to ensure that there is no threat of rapid progression if they are left untreated. Consequently AS patients represent a clinically homogenous group.

Paradoxically, the psychological heterogeneity of this specific patient cohort is likely to be large. For example, a man recently diagnosed with localised PCa who is being managed with AS and is awaiting his first six month PSA test may be experiencing relatively high levels of distress. This distress may be a factor of coming to terms with their diagnosis, fear of unchecked cancer progression, their upcoming PSA test or a combination of these issues.

Conversely, for a PCa patient who is being managed with AS for localised PCa that was diagnosed five years previously, the situation may be very different. For such a man to have remained on AS for such a substantial period of time would mean that they have not experienced any meaningful levels of disease progression, have a highly stable malignancy, are likely to be asymptomatic and are not likely to have encountered any negative impacts upon their general life and wellbeing as a result of their diagnosis (Pickles et al., 2007). It is likely that such a patient would present with very low levels of psychological distress.

Both of these men have received the same diagnosis and are undergoing the same treatment protocol, but to understand their greatly varying levels of distress, one must place their individual circumstances into context, with specific focus on time since original diagnosis.

Research suggests that the greatest upheaval in psychological health within the PCa community occurs within the first 12-15 months post-diagnosis (Hedestig, Sandman & Widmark, 2003; Pickles et al., 2007). If the majority of the patients contacted in the current investigation had been diagnosed several years ago, they may have been experiencing very little distress and thus saw no benefit in recruiting into a support programme to help them manage such issues.

6.5.3. Recruitment Methodology Critique

In trying to understand why I was unable to recruit a suitably sized sample of AS patients into the current investigation, it was important to review and critique my recruitment processes to determine what impact they may have had upon recruitment.

The first contact potential participants had with the investigation was through the Patient Information Pack (PIP). Included within the PIP was a Patient Invitation Sheet (PIS). The PIS provided the participants with a detailed overview of the study, what taking part would involve, the time requirements required and an explanation and overview of MBSR.

Through retrospectively reviewing the PIS, its content and the way in which it was worded, little room for alteration was observed. As discussed previously, the predominant reason for participants deciding to not recruit into the investigation was the excessive time demands required. Yet it was an ethical prerequisite to ensure that all of the logistical demands of the investigation were clearly and transparently described in the PIS. Whilst this may have appeared daunting and possibly off-putting to the participants, and thus may have had an instant and direct impact upon their decision to not take part, there was unfortunately little scope for a different approach to be taken due to the ethical constraints imposed upon such recruitment procedures.

One possible alternative to this may have been to use a different recruitment process that removed the need for the PIS. Such a process could have involved contacting potential participants first without having sent them a PIP. However, such an approach was unlikely to have received ethical approval as it would involve contacting patients directly without having asked for consent to do so.

6.5.4. Strengths of the Research

The methodological rationale and design of the current investigation was based upon the evidence of previously conducted research highlighting the effectiveness of MBSR in the management of psychological distress in cancer patients (Carlson et al., 2003; Carlson et al., 2007; Carlson & Garland, 2005; Garland et al., 2007). As such this methodological approach was robust.

On initiating the recruitment process it quickly became apparent that for this specific cohort of patients, MBSR was deemed an unacceptable intervention. During the recruitment process, all

non-responders were contacted by telephone to further assess their desire to take part in the study. As overviewed in the results section, over the course of these telephone conversations it became apparent that the majority of these men (81%) were experiencing a relatively high degree of psychological distress and felt that they had little information about their diagnosis, their treatment and any future progression to radical treatment, all of which was causing them distress and concern.

Despite such concerns, these men were still not willing to commit to the 8-week MBSR intervention that may have offered them a degree of support in terms of helping them better manage their distress. The apparent principle reason for this was that the time and travel demands of the programme were too demanding.

In light of such feedback, I decided to terminate the recruitment process in the realisation that I would be unable to recruit a meaningful sample of AS patients into the MBSR programme, ensuring that no further time or resources were wasted upon this recruitment process.

Whilst the inability to recruit was frustrating, it was successful in allowing me to see that a prolonged and time consuming support intervention such as MBSR is not likely to be an acceptable form of support for PCa patients being managed with AS and that a different approach will most likely be needed.

6.5.5. Relationship to the Previous Research

Unfortunately, only a relatively small foundation of research into interventional studies aiming to manage psychological distress in the PCa community currently exists, as overviewed in Chapter 5. What research does exist is also unclear and contradictory. For example, Penedo et al., (2004) observed that PCa patients who had been radically treated with either surgery or radiotherapy experienced significant improvements in both general and PCa specific quality of life as a result of taking part in group support.

Similarly, in a large national survey into the benefits obtained by attending group support, Steginga et al., (2005) observed that PCa patients experienced higher levels of satisfaction with their treatment and treatment related decisions and experienced a higher quality of life as a result of their participation in group support. They also expressed that sharing experiences with other men offered them a degree of reassurance which in turn helped alleviate distress and anxiety.

Conversely, there are reports that support groups may have a detrimental effect upon PCa patients. For example, Chapple & Ziebland (2002) interviewed 52 PCa patients to generate information on what factors impacted upon their treatment decision making process. It was observed that men who were being managed with watchful waiting who attended support groups were put under considerable pressure during group meetings by the other members who were receiving radical treatment to do likewise, leading to additional anxiety and uncertainty as to whether they should instigate radical treatment themselves.

A strong foundation of research exists to highlight the benefits of group based support interventions as a tool to manage psychological distress in female cancer populations (Meneses et al., 2007; Antoni et al., 2006). Yet given the reported inaccuracies of generalising empirical psychological research findings from one cancer population to another (Balderson & Towell, 2003), and from one gender to another (Massie & Popkin, 1998) it is unlikely that such benefits are directly transferable to male specific cancer sites such as PCa.

Based on the conflicting research evidence and the findings from the current investigation, it is clear that if we are to design support interventions that are to be effective at managing distress within the AS community, whilst at the same time being deemed acceptable enough to recruit into, a much clearer understanding of the subjective needs and wants of this patient cohort is necessary.

6.5.6. The Way Forward

To address this issue and allow for the design of an AS specific support intervention, it is fundamental that the specific subjective needs of this population of AS patients, in relation to their supportive requirements, be more clearly understood and defined. The limited foundation of research within this area means that we currently have very little understanding of what the content and format of these interventions should be to maximise effectiveness, recruitment and adherence. More specifically, do AS patients prefer group based interventions or private ones? Do they want purely emotional support, purely clinical support, purely educational support or a combination of these? Do they want the sessions to be led by other patients or clinical experts?

To move towards finding answers to such questions, I planned to undertake in-depth qualitative interviews with a sample of twenty PCa patients being managed with AS. The interviews were designed to elicit a much greater understanding of the issue of psychological

and emotional distress in AS, what causes it and how best we could help them manage it in terms of the design, content and delivery of an AS specific support intervention.

6.5.7. Conclusion

The key aim of this study was to assess AS patients willingness to recruit into a standard 8-week MBSR intervention. The findings suggest that AS patients are not interested in nor willing to recruit into such an intervention. A variety of reasons exist to explain this disinterest, the most predominant of which was the demanding time commitment required.

Unfortunately, due my inability to recruit a suitably sized sample of AS patients into this study, it was not possible for me to address the other key research aims of this investigation that were alluded to in the introduction.

From a qualitative perspective, it is still unknown what AS patients' beliefs and experiences of MBSR are and how it may be possible to modify the standard 8-week programme to make it more appealing to this patient group. Likewise, from a quantitative perspective, it is still unknown what impact an 8-week MBSR intervention would have on anxiety, depression, stress and coping among a cohort of AS patients.

The current study has highlighted that PCa patients being managed with AS are not willing to recruit into a standardised MBSR programme being offered to them as a tool to allow them to better manage psychological distress. Given the growing foundation of research highlighting the impaired psychological health of AS patients (Burnet et al., 2007; Latini et al., 2007; van den Bergh et al., 2009), and the important clinical ramifications of such impairments (Patel et al., 2004; Latini et al., 2007), it is crucial that support programmes that are deemed acceptable to this patient group to recruit into are designed and trialled to allow AS patients to better manage any distress they are experiencing.

Chapter 7

A Qualitative Feasibility Study into the Design of a Psychological Support Intervention for Managing Distress in Prostate Cancer Patients Managed with Active Surveillance

7.1. Research Question and Aims

Research Question: What problems and concerns do PCa patients being managed with AS experience and how can we best design a support intervention to allow them to better cope and manage such issues?

Aims:

1. To assess AS patients' experiences of living with AS.
2. To identify any problems and concerns AS patients have or have had as a result of AS.
3. To determine what kind of support AS patients need, want and would be willing to take part in to allow them to better manage any problems or concerns they are experiencing.

7.2. Introduction

A recent study conducted as part of this thesis (Chapter 4) highlighted a depression and anxiety prevalence of 12.4% and 23.3%, respectively, from a cohort of over 300 AS patients. These data suggest that those on AS are three times as likely to experience anxiety and twice as likely to experience depression as the general population of over 65's in the UK (Department of Health, 2011). In light of the significant impact of anxiety as a predictor in determining which AS patients will transfer to unnecessary radical treatment (Patel et al., 2004; Latini et al., 2007), these findings are important.

The mechanisms underpinning AS patients desire to initiate radical treatment which might be deemed unnecessary in clinical terms is heavily grounded in psychological theory. One of the key stressors faced by cancer patients is uncertainty (Sammarco, 2011; Koch et al., 2014). This is particularly true for AS patients (Bailey et al., 2004; Kazer et al., 2011). This can encompass uncertainty about treatment, recovery and mortality. Based upon Mishel's Uncertainty in Illness Theory (Mishel, 1990), uncertainty only becomes undesirable when the individual believes that the outcome associated with such uncertainty will be negative. A patient's belief

in the inevitability of a negative outcome stems from the resources they have at hand to help them cope with the uncertainty. Therefore uncertainty only becomes stress and anxiety inducing when the demands of the situation exceed the patient's resources to cope (Lazarus & Folkman, 1984).

Gender studies into masculine based coping mechanisms show that men are highly effective at putting into motion problem-focused coping strategies (Nicholson, 2000; Kiss & Meryn, 2011). Problem-focused coping strategies can be applied when the individual can initiate a clearly defined, objective and definitive solution to a given problem. For example, for AS patients with localised PCa, problem-focused coping strategies could entail the initiation of surgery. This definitive coping strategy would remove both the problem (i.e. the prostate cancer) and the anxiety associated with it, even though surgery may represent a clinically unnecessary procedure that is associated with long term sexual and urinary dysfunction (Wilt et al., 2012; Bacon et al., 2002).

However, in situations when problem solving strategies are less likely to be successfully engaged, the patient must rely on emotion-focused coping strategies. This involves dealing with the emotional concomitants of the stressor itself rather than trying to remove it. If the individual does not have the supportive resources at hand to do so, they are likely to experience progressive and debilitating psychological distress until such a time as a problem-focused coping strategy can be implemented as a last resort. For example, if an AS patient was experiencing chronic and progressive anxiety and stress as a result of living with an "untreated" cancer and did not have the resources to effectively manage these conditions, the patient may over time feel that he has no option but to initiate an effective problem-focused coping strategy and opt for radical treatment.

When living with AS, it therefore becomes essential that men are empowered with emotion-focused coping strategies and resources that they can call upon and implement to allow them to better manage the uncertainty, stress and anxiety they are experiencing as a result of AS. This in turn may help to prevent anxious men from transferring to radical treatment (Pickles et al., 2007). Research into the development of interventions that aim to equip and empower AS patients with self-care techniques that will allow them to effectively manage psychological distress with emotion-focused coping strategies should be viewed as an issue of paramount importance for those working within the field of PCa.

In a previous attempt to develop such an intervention, I aimed to recruit a sample of AS patients into a Mindfulness Based Stress Reduction (MBSR) intervention. Unfortunately I was

unable to recruit a suitably sized sample of men into this intervention, as overviewed in the previous chapter. Therefore if we are to be effective at developing a disease specific support intervention for AS patients, it is imperative that we determine exactly what kind of support and help these patients want, need and would be willing to participate in. Given the current lack of research and understanding within this area, a detailed qualitative approach was deemed to be best suited to this task.

The foundation of qualitative research into the needs of AS patients is sparse. The research that does exist reports that AS patients experience feeling alone with their disease, living under constant and persistent uncertainty which was viewed as a threat whilst experiencing fear, anxiety and worry (Hedestig, Sandman & Widmark, 2003). Whilst such research is important in allowing us to understand the psychological and emotional burden of AS, it provides limited insight about what specific kinds of support AS patients would like to support them better.

It is not currently known or understood what the patient centred requirements of this group of patients are in regards to what they need to help them better manage the demands of AS through the provision of emotion based coping strategies rather than problem based coping strategies. What type of intervention, in terms of structure, content and format, do they want? How can we maximise effectiveness, recruitment and adherence? Are these men likely to prefer group based interventions or private ones? Are they likely to want purely emotional support, purely clinical support, purely educational support or a combination of these? Are they likely to want the sessions to be led by other patients or clinical experts?

Utilising an in-depth qualitative approach would allow me to answer these questions and generate vital, patient centred information into the specific information and supportive care preferences of this group. Once such information becomes available, it can be used to inform the design of a patient centred, focused and disease specific support intervention that will provide AS patients with the information and self-management techniques needed to better manage the uncertainty and distress often associated with AS in a structure and format that is acceptable to them. Such an intervention specifically for PCa patients being managed with AS will be the first of its kind to be designed within the UK.

The aim of the current investigation was to address this issue and conduct a series of semi-structured qualitative interviews with a sample of AS patients to elicit an understanding of the

psychological and emotional distress faced by these men, what causes it and how best we could help them to manage it.

7.3. Methods

7.3.1. A Qualitative Approach

Why Qualitative?

The primary aim of the current investigation was to improve the understanding of AS patients' views on the psychological and emotional burden of being managed with AS and how it may be possible to support these patients to allow them to better manage this burden. To allow me to do so, data generated from a different epistemological tradition to the "hard facts" associated with positivist research was required. As I was concerned with understanding the lived experiences, interpretations and perspectives of men living with and being managed by AS, a qualitative interpretive approach was deemed most appropriate (Green & Thorogood, 2011). Adopting such an approach would allow me to generate findings that would show an understanding of the world from the perspective and point of view of AS patients themselves rather than simply trying to "explain" the problems of AS. Utilising a qualitative approach in this way would allow for the generation of a rich subjective understanding of the lived experienced of men being managed with AS.

Why Interviews?

Qualitative research compromises a variety of different methodologies that include observation, textual analysis, interviews and transcripts (Green & Thorogood, 2011). As I was primarily concerned with generating an interpretive account of AS patients' views and experiences, utilising an interview approach was deemed the most appropriate methodology. The use of in-depth, semi-structured interviews was the most effective means of allowing me to explore and understand the subjective causes of distress in men being managed with AS and how it may be possible to design support interventions to address and manage this distress. By using semi-structured interviews I was also able to impart a degree of "flexible" control over the course of the interviews to ensure that I was asking questions that would allow me to reach my research aims.

Why Thematic Analysis?

Many forms of qualitative analyses exist and the choice of which one to adopt must be guided by what the researcher wants to know and by the research question they are investigating (Silverman, 2011). Approaches such as grounded theory, discourse analysis and conversation analysis are all married to a specific theoretical position and operate within a specific theoretical framework, for example, the generation of theory about any given issue. However, these approaches should only be employed when one wishes to specifically develop a theory around the issue in question (Mays & Pope, 2000). In the current investigation, it was my aim to better understand the lived experiences of AS patients. It was not my intention to produce a comprehensive grounded theory of such issues. In areas of research such as this which have been substantially under-researched and need to be more broadly documented and understood before theory generation is initiated, thematic analysis (TA) has been shown to be a particularly useful form of analysis (Mays & Pope, 2000; Pope & Mays, 2006). Consequently I decided that a TA methodology would provide me with the ideal approach to utilise in the current investigation. A detailed overview of the methodological process of TA can be seen in 7.3.4 below.

7.3.2. Recruitment and sampling

Eligibility criteria

Participation in this study was limited to men who fulfilled each of the following criteria:

Patient Inclusion Criteria

- A positive, biopsy confirmed diagnosis of PCa.
- Diagnosis at least 2-months prior to the participant's inclusion into the study to allow any initial post-diagnosis mood disturbance to dissipate.
- Undergoing AS as their primary treatment option at the time of recruitment.
- Fluent in the English language.

Patient Exclusion Criteria

- A positive diagnosis of a second cancer other than PCa.
- Additional significant comorbidity (physiological or psychological) that may negatively impact upon mood state.

Recruitment Procedures

In order to fulfil the aims of this investigation, participants were recruited from the PCa clinic at Southampton General Hospital utilising a criterion basedsampling approach under the guidance and supervision of Mr Brian Birch (Principal Investigator and lead consultant

urologist). This sampling strategy ensured the selection of information rich cases who could speak about their experiences of living with and being managed by AS (Patton, 2002).

When planning the methodology for this investigation, it was decided upon in conjunction with my qualitative supervisor that my minimum recruitment target needed to be 20. This figure was decided upon for two key reasons:

1. Pragmatically, there were only 32 AS patients on the clinic records when I opened recruitment so aiming for a minimum of 20 was a realistic target.
2. Methodologically, it is generally accepted that with a sample of 20 participants one will reach saturation with in any given topic area with a sample of around 20 participants (Patton, 2009).

Whilst my aim was to recruit more than 20, this figure represented the minimum figure required to produce a meaningful and useful data set.

Patients were initially identified through the screening of patient records to identify suitable patients who qualified for inclusion into the study based on the pre-determined inclusion and exclusion criteria.

Once the records had been screened, a full list of eligible patients was drawn up. Each patient was then sent, by post, a Patient Information Pack (PIP; see Appendix 13) which included:

I. Patient Invitation Letter (PIL) – The PIL provided the participant with a brief overview of the investigation and informed them of what to do next should they wish to take part.

II. Patient Information Sheet (PIS) - The PIS provided a detailed introduction and overview of the investigation, informing each participant of what their involvement would entail should the decide to take part, who was conducting the research, their rights as a participant and who to contact for more information.

III. Patient Reply Slip (PRS) – The PRS provided the participant with a means of informing the research team that they would, or would not, like to hear more about the investigation.

IV. A Freepost return envelope – This was included within the PIP to allow the participants to return the PRS to the research team at Aldermoor Health Centre.

Once the PIP's had been mailed out, I waited one week before identifying all non-responders. Each non-responder was then contacted once, by telephone, to enquire into whether or not they would like to take part in the study. If they did, they were asked to return the PRS as per the instructions listed in the PIL, if they still had it. If they did not then the patient was re-sent

a PIP to ensure they had a copy of the relevant information and they were asked to re-read this and then send in the PRS if they still wished to partake in the study. Completing and sending in the PRS indicated initial consent for me to contact the participant by telephone to describe the study in greater detail and to answer any questions the patient may have had.

Once all the PRS's had been received, each patient was contacted and given a detailed verbal overview of the study by telephone. The purpose of this was to answer any questions the patient may have had and to ensure that before consenting to partake in the study the patient was fully informed of what they would be undertaking. During this telephone call, I scheduled a date and time that was convenient for the patient to conduct one face to face interview. The patient was given the opportunity of conducting the interview in their own home or at Aldermoor Health Centre. In a bid to maximise recruitment, if it was not possible to organise a convenient time to conduct a face to face interview, the patient was asked to conduct the interview over the telephone.

7.3.3. Interview Procedures

Full ethical approval for this study was granted by the Oxfordshire Research Ethics Committee on 16th June, 2013 (REC 11/SC/0355; Appendix 14) and all interviews were conducted with appropriate ethical and research governance guidelines. Sponsorship and the necessary insurance requirements were provided by the University of Southampton.

Before the interviews began the participants were talked through the Patient Information Sheet to ensure that they fully understood the nature and purpose of the interview. During this conversation it was reiterated that the interview would be digitally recorded, the file of which would be fully anonymised and securely saved on a University of Southampton computer and that all information would remain strictly confidential. The participant was informed that the interview would last for between thirty and ninety minutes, that they were at liberty to stop the recording at any time and were free to not answer any of the questions asked over the course of the interview and indeed could terminate the interview at any time and for any reason. Before commencing the interview, participants reconfirmed that they had consented to take part and that the interview would be anonymously recorded.

An interview guide was created prior to the initial pilot interview to ensure that all of the keys domains that I wished to cover during the interview were clearly listed. This acted as a prompt during the interviews and ensured that I was able to impart a degree of structure over the direction of the interviews. This interview guide was then utilised during the pilot interview

(see below). After the completion of the pilot interview the interview guide was modified to ensure that any questions that were perceived to be ambiguous or unclear were modified to help improve the "flow" of the interview. The final interview guide was checked and approved by my qualitative supervisor.

One pilot interview was conducted with a medical homeopath who did not have PCa. The purpose of this interview was to gain experience in asking the pre-set interview questions to ensure that I felt comfortable and ready to conduct future interviews with PCa patients. Although this interview was not conducted with a PCa patient, using a medical doctor ensured that the answers provided were in keeping with and sympathetic to those I could expect from PCa patients. This was aided by the fact that the doctor interviewed was a sixty six year old man and thus in the same age bracket to many of the PCa patients I would be interviewing. This process was an important part in developing my knowledge of and sensitivity towards the issues faced by PCa patients being managed with AS.

Following the piloting process, interviews with the recruited AS patients began. Upon switching on the digital recorder, the interview began with a grand tour question (Spradley, 1979) that would elicit insights about each individual's cancer journey. An example of the opening question follows:

"Please describe how this all started and how you came to be diagnosed with prostate cancer in the first place?"

During the interview I kept a note pad open to write down key words, phrases or points that the participant made that I wanted to revisit later in the interview. Prior to and after the completion of each interview, reflexive notes were made about the interview. This was done to ensure an iterative process of learning and to allow for the modification and tailoring of the interview questions. As with all qualitative research, the researcher and their beliefs play an important part in the research process and the results generated. The keeping of a detailed and fully transparent reflexive diary with entries prior to, during and after the completion of each interview allowed me to develop a much greater insight into the interview process and my role in it. It was hoped that through doing so, my inevitable subjectivity would become a valuable and insightful resource rather than a hindrance (Holloway, 2006). A more detailed overview of methodological rigour and reflexivity can be seen in 8.2.6 below.

7.3.4. Data Analysis

The following provides an overview of the methodological steps involving in conducting TA as recommended by Braun & Clarke (2006).

Stage 1: Data familiarisation

The digitally recoded interviews were sent to a professional scribe for transcription into written form immediately after the completion of the interview. Transcripts were produced in an orthographic or verbatim manner and included all verbal and non-verbal utterances (i.e. signs and pauses). Each hard copy transcription was received back within 5-days of being sent off. Once the hard copy transcription was received, data analysis began. Performing data analysis as soon as possible after the completion of the interview represents good qualitative practice (Silverman, 2011) as the interview, and the processes inherent to it, remain fresh in the mind of the interviewer.

The first phase of the data analysis process involved repeated readings of the transcripts to maximise familiarity with the content, context, depth and breadth of the data. By reading through each transcript twice before beginning the "formal" analysis process, I was able to immerse myself in the data, allowing me to identify and contextualise meanings, patterns and key phrases and words, all of which were noted down on each transcript. If during this familiarisation process it was difficult to contextualise or clearly understand any of the statements or comments made by the interviewee from the hard copy transcript, the audio file of the interview was listened to, to help clarify such issues.

Once this initial familiarisation process was completed and I felt comfortably immersed in the data, the more formal coding processes could begin.

Stage 2: Generating initial codes

Generating the initial codes involved carefully reading through each transcript and highlighting features of the data that were interesting and/or relevant to my research questions along with any unexpected emergent features amongst the data. Coding was conducted manually by hand. As I worked through the transcript, coloured highlighters were used to "pick out" sections of the text that I wished to code. As the analysis was utilising a predominantly 'data-driven' rather than 'theory driven' approach, coding was performed in a systematic and inclusive line by line manner to ensure that the full data set was coded. Full and equal attention was applied across the full data set to ensure that no data were missed. During the coding process it was also important to place the individually fragmented codes in context with

the data that surrounded it. This was an important issue to address as it is a common criticism of line by line coding that important contextual meaning can be lost. An example of line by line coding can be seen in Figure 9.

Figure 9: Line by line coding example

Interview 19 Extract	Line by Line Coding
I had done a lot of reading and certainly a lot of the literature, especially from America where they are very keen on surgery, active surveillance is looked upon as a recipe for disaster. By the time they find there's something gone wrong, there is very little that can be done, but that is in books written by surgeons.	Patient had done a lot of reading. Active surveillance looked upon as a recipe for disaster in the American literature. By the time something goes wrong, little can be done about it. Aware that this point of view is from surgeons

It was also important to differentiate between codes that were defined by me as the researcher and in-vivo codes which used the participants own words. Once the transcript had been systematically coded on a line by line basis, a coding document was created. This involved extracting each of the codes highlighted in the transcript and listing them on a line by line basis in a Word document to create a complete list of codes for the entire data set. At this point it was possible to progress to the next stage of analysis.

Stage 3: Searching for themes

The aim of this stage was to refocus the analysis in a much broader manner by trying to develop initial themes from the individually listed codes produced in Stage 2. Doing so involved reading and re-reading the codes listed in the coding document and creating a series of broad themes that could then encompass all of the individual codes identified. This was done by manually cutting out each of the codes listed in the coding document and creating piles of similar codes. Once each individual code had been assigned to a pile, each pile was given a tentative name that accurately described the codes it contained (Figure 10 below).

Figure 10: Sub-theme and theme generation.

Initial Codes	Sub-Theme	Theme
- At least I know where I stand. - It's being monitored. - Somebody's interested, they are checking on me. - If medical people say that for you AS is the best option, you believe them and you go along with it - I was quite happy with AS.	Positive aspects of active surveillance	**Patient Views Towards Active Surveillance**
- Well if something can be done, prior to it becoming severe, well why isn't it being done. - I don't think the surveillance is done enough. - There is not enough support which is worrisome and concerning. - By the time you find there's something gone wrong, there's very little that can be done.	Negative aspects of active surveillance	

Once each theme had been identified and labelled, it was then possible to see how each theme related to each other. At this point it was necessary to see whether any of the listed themes could be further broken down into sub-themes that could be collectively grouped together and encompassed by a dominant theme. At this point it was possible to progress to the next stage of analysis.

Stage 4: Reviewing themes

Stage four involved refining the initial themes and sub-themes developed in the previous stage to ensure that all of the data encapsulated within each theme fitted logically within that theme and was distinct from the other themes.

Analysis at this stage had two clear levels and followed the TA guidelines generated by Braun & Clarke (2006). The first level involved referring back to the codes used to form each theme to make sure that they logically belonged and fitted there. It was also important to ensure that a coherent pattern existed between all of the codes making up a theme and that there were no

'deviant codes' that had been entered into a theme but on second analysis clearly did not belong there. In instances where this was the case, the deviant codes were extracted and entered into another theme to which it was more suited. If the deviant code was deemed too "isolated" or irrelevant it was listed as a deviant case. This process also allowed for the identification of themes that didn't actually constitute themes, themes that could be collapsed and integrated into another similar theme and themes that contained so many important sub-themes that it was necessary to re-classify the data into two individual themes.

Utilising this approach in an iterative manner allowed for the creation of a series of themes and sub-themes that encapsulated relevant codes in a logical and coherent pattern. At this point it was possible to progress to the second level of Stage 4 analysis.

Level two analysis followed a similar process to that performed in Level 1 but on a broader level. This involved ensuring that the themes and sub-themes that were revised in Level 1 were valid in relation to, and indicative of, the entire data set and that they reflected the overall nuance of the interview. During this process it was necessary to re-read the full transcript to ensure that the themes created worked and made sense in relation to the full corpus of the interview in a meaningful, insightful and contextual manner.

Stage 5: Refining and naming themes

The fifth and final stage of the data analysis process involved refining and naming the themes and sub-themes that had been re-worked and created in the previous stage to a point that the initial results could be produced and the write up could begin. This stage of the analysis centred upon focusing on the "essence" of what each theme was about in relation to the research question and ensuring that each of the themes were directly related to the aims and purpose of the study in a meaningful way. It was also crucial to ensure that the titles given to each theme clearly articulated what the theme encapsulated.

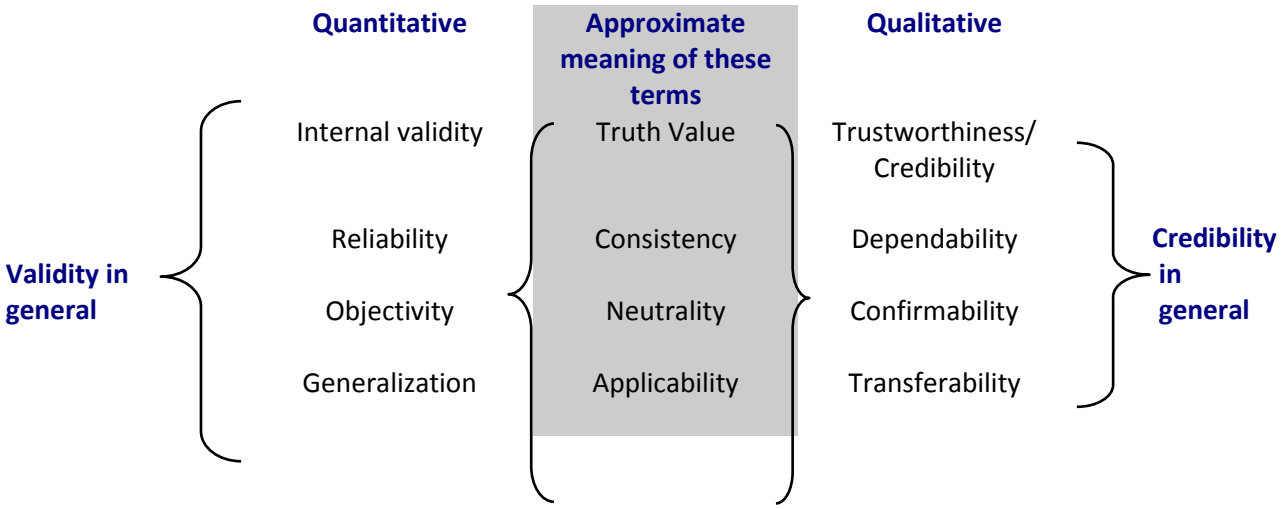
7.3.5. Validity and Rigour

Although now much less common, qualitative research is often viewed as anecdotal and unsystematic. Hamberg et al. (1994) suggested that these kinds of criticisms are often based on the canonical standards of scientific 'strictness' or rigour associated with the hypothetico-deductive paradigm, such as internal validity, objectivity, reliability and generalization.

While there are significant debates in the qualitative community about the extent to which researchers should focus on 'quality criteria', most agree that certain issues and standards

need to be in place to produce 'credible' research. Some qualitative researchers use a similar language to that used by quantitative researchers, while others use different 'indicators' or words to describe rigour in qualitative research, as overviewed in Figure 11:

Figure 11: 'Scientific Rigour in Qualitative Research'. (Hamberg et al., 1994).



A number of factors need to be in place to create credible and trustworthy research and this involves evidence of attention to each of the following issues:

Transparency: Detailing and documenting a transparent and honest account of the procedures undertaken during the qualitative research process represents a benchmark of qualitative methodological rigour (Hiles & Cermak, 2007).

I aimed to maximise methodological and analytical transparency by clearly documenting every stage of the investigative process, from the conducting of the interviews through to the critical evaluation of the finalised results. For example, interview recordings were transcribed in full to ensure that the context of the questions raised and the answers produced were not lost. Likewise, during the initial data analysis, a full paper based audit trail was maintained to clearly signpost how initial codes and sub-themes were developed. Regular supervision meetings were also attended and documented to ensure that the codings and sub-themes produced were reviewed and agreed upon by an experienced qualitative researcher.

As with all qualitative research, documenting and accounting for reflexivity is a key methodological issue. As previously mentioned, a detailed reflexive diary was maintained across the entire interview process to ensure that my subjective views towards, and impacts upon, the course of the interviews were documented in a transparent manner.

For example, if I became aware during the interview that I had asked a question relating to a key issue (i.e. levels of anxiety or uncertainty) and then I asked another similar question again to try and get the patient to further elaborate on these issues that we important to me, I noted down in my diary a short statement such as “pushing the point” and referenced this against the time on the digital recorder so that I would know where abouts in the interview this occurred. This allowed me to see when and where I was trying to get the patient to talk about issues that were important to me rather than him and thereby impacting upon the “flavour” of the interview. During the subsequent data analysis and when listening to the audio files and reading the transcripts, referring back to the diary allowed me to see where my own opinions and biases may have impacted upon the interview.

Likewise, after each interview had finished I spent 10-15 minutes writing out notes on how I felt the interview had gone and in particular the impact I had had upon the direction and flavour of the interview and where I had possibly pressed too hard or not hard enough on any given topic of importance. Over the course of several interviews I sometimes saw patterns emerging, particularly around the key issues of AS and PSA monitoring where I was pressing hard for more and more information around this area. The diary allowed me to identify this, account for it and learn from it to ensure that similar mistakes were not made in the subsequent interviews.

A more detailed overview of how reflexivity was addressed follows.

Reflexivity: Throughout the course of the study, it was important for me to critically reflect upon how my own views, beliefs and biases impacted upon the interview process, the collected data and the generated results. Inevitably my gender, personal experiences of family members with PCa, research biases and my experience as a researcher impacted upon the direction and ‘flavour’ of each interview. If such issues are accounted for and transparently documented, they can add depth and meaning to the generated findings rather that detracting from the accuracy of them.

To ensure that a reflexive approach to data collection and analysis was adopted, I used and maintained a detailed reflexive diary throughout the interview process. This was utilised to document any concerns or thoughts I had prior to each interview, to note any key points or observations that I made during the interview regarding my impact upon the questions and answers generated and to summarise after the completion of each interview my thoughts and feelings about how the interview had progressed and developed.

In particular, the reflexive diary allowed me to note down during the interviews where and how my own motivations and beliefs about the study had impacting upon the interview. For example, my immersion in the research relating to psychological distress in PCa, and indeed the results generated from the investigations overviewed in chapters three and four of this PhD, may have biased my belief that each and every PCa patients would be experiencing psychological distress. The risk of such a preconception was that I was subconsciously coercing the patients into discussing issues relating to distress rather than on issues that were more salient to them. By documenting such issues, I was able to use my reflexive observations to guide and inform both the subsequent interviews and to inform and add context during the data-analysis process.

Additionally, it has been observed that subjective and individualised reflexivity is relatively limited as one is not able to be fully aware of all the ways in which one's subconscious assumptions impact upon the interview process (Seale 1999). To address this, it was important to use regular supervision meetings to allow informed third persons to critique and challenge any of the judgements and assumptions I made.

Trustworthiness/Validity: Ensuring the validity of qualitative research findings is a problematic issue based upon the inherently subjective nature of the research. Despite this, it is important that the methodological and analytical procedures undertaken help to maximise the "truth, value and authenticity" (Holloway, 2006) of the generated results as a way of answering the reader who asks: "why should I believe these results?"

In a bid to address such issues and to help maximise validity, several safeguards were utilised. Firstly, it is a common and justified criticism of qualitative research that the researcher simply picks out and reports "juicy" anecdotes that support the research question (Green & Thorogood, 2011). To ensure that anecdotalism did not occur within the current analysis, constant comparison was utilised to help identify deviant cases that did not fit the themes and sub-themes generated. If, during the data coding stage, deviant cases were identified, they were clearly highlighted and labelled to allow the deviant cases to be transparently identified and documented. This ensured that the full data set for all twenty interviews were systematically analysed and reported.

Secondly, simple counts of the codes making up the sub-themes were performed to provide perspective on how prevalent such codes were (Green & Thorogood, 2011). This helped to ensure that when generating the results, it was possible for the reader to quickly determine

how many of the twenty men interviewed made reference to any given topic, which in turn added depth and context to the importance and severity of the said topic. For example:

Sub Theme - Positive Aspects of Active Surveillance: "Four men described being happy with the concept of PSA monitoring…"

Simple counting approaches such as these allow the reader to personally determine how many men were happy with AS rather than relying on the subjective and possible anecdotal reporting of the researcher.

The final approach utilised to help safeguard validity involved employing respondent validation checks during the interview sessions (Braun & Clarke, 2006). To do so, I provided a brief verbal summary of the answers provided to me by the interviewee after each set of questions. I then asked the interviewee whether the summary I provided was an accurate overview of what they had both said and meant over the previous round of questions. If the interviewee agreed, it provided an accurate indicator that the interviewee responses being recorded were a valid representation of their true beliefs, views and opinions, a process that greatly added to the trustworthiness of the data collected.

Dependability/Reliability: Within qualitative research, the concept of reliability refers to the "likelihood that a similar piece of research would elicit similar kinds of themes" if undertaken by a different research team (Green and Thorogood, 2011).

Ensuring reliability within the current investigation involved a certain degree of overlap with some of the other measures of methodological rigour described above. These included developing a comprehensive and fully transparent audit-trail along with using frequency counts to ensure that the themes and sub-themes developed were reliable and indicative of the overall flavour of the interviews and not "cherry picked" examples to support my own personal views and opinions.

One additional methodological approach utilised to further optimise reliability was to use multiple coders during the data-analysis stage (Braun & Clarke, 2006). Two researchers, one of whom was part of the investigation in a supervisory role and one who was fully independent of it, individually read and coded 7 transcripts. The codes they identified were then compared with those created by myself as the main investigator to check for both consistency and accuracy across the coding spectrum. This allowed for the identification of areas of agreement and disagreement between us. Areas of disagreement were discussed and modified until a new universal agreement was reached about the codes created.

7.4. Results

7.4.1. Participant Characteristics

Twenty men out of an approached sample of 32 (response rate: 62.8%) with a biopsy confirmed diagnosis of PCa who were being managed with active surveillance (AS) were recruited into this study and completed their interview. 14 participants completed and returned the Patient Reply Slip sent out as part of the Patient Information Pack stating that they wished to take part in the investigation. The remaining 18 participants were contacted by telephone to enquire into the willingness to recruit into the study of which six agreed to take part, bringing the recruitment total to 20. Across these 20 men, their mean age was 69 years (range 55-79) and all were of white British ethnicity. Summary characteristics of the participants can be seen in table 11 below.

Table 11: Summary characteristics of the recruited participants.

Patient ID	Age	Time since diagnosis	Relationship status	Educational status	Ethnicity
1	71	6	Married	Secondary Education	White British
2	68	3	Married	University	White British
3	55	2	Married	College/Specialist Training	White British
4	75	4	Married	College/Specialist Training	White British
5	72	3	Co-habiting	Secondary Education	White British
6	70	4	Married	Left school <15	White British
7	59	3	Married	Left school <15	White British
8	70	5	Married	Secondary Education	White British
9	74	1	Divorced	Secondary Education	White British
10	68	3	Married	Left school <15	White British
11	69	3	Married	Secondary Education	White British
12	58	1	Married	Secondary Education	White British
13	71	4	Married	Secondary Education	White British
14	78	4	Widow	College/Specialist Training	White British
15	69	3	Married	Secondary Education	White British

16	72	6	Widow	Secondary Education	White British
17	71	3	Married	University	White British
18	71	2	Married	University	White British
19	69	3	Married	College/Specialist Training	White British
20	72	5	Married	College/Specialist Training	White British

7.4.2. Interview Overview

The aim of the current study was to generate information about the degree of psychological distress experienced by men being managed with AS and to elicit a greater understanding of what kind of support these men wanted to allow them to better manage such distress.

Across the 20 interviews, 18 were conducted face to face whilst 2 were conducted over the telephone. In both of these cases, telephone interviews were decided upon as the participants were unwilling to have me come to their home or meet up in person to conduct the interview. To prevent losing these men from recruitment, I asked if they would be happy to be interviewed over the telephone which in both cases they were. The length of the interviews varied from 36 minutes to 72 minutes with an average length of 53 minutes.

The systematic analysis of the interview transcripts in the manner previously described in the methods section resulted in the generation of two overarching themes labelled as follows:

Theme 1: "The safety net has a hole in it" – problems of living with PCa and being managed with AS

Sub-Theme 2.1: PSA monitoring

Sub-Theme 2.2: Active surveillance

Sub-Theme 2.3: Emotional/psychological problems

Sub-Theme 2.4: Physical problems

Theme 2: Managing life/survivorship under AS

Sub-Theme 3.1: Group based support interventions

Sub-Theme 3.2: Supporting emotional/psychological health and wellbeing

Sub-Theme 3.3: The structure and design of group based support interventions

Sub-Theme 3.4: The role of the internet

7.4.3. Contextual Information and Sample Description

When asked, several of the men described how physical symptoms had led them on to the road of eventual diagnosis. In all cases, the physical symptoms centred on urinary function:

"I started having problems, getting up a lot of times in the night and going to the loo and thinking something was obviously going wrong" (P1, 9-11).

However, in most cases, men were diagnosed via a routine blood test which highlighted an elevated PSA which in turn led to a urology referral and subsequent diagnosis:

"The GP said I haven't seen you for a long time and being over 60 I think you ought to have an MOT. I said – yes, go on then, so he booked me in for a blood test and when he got the results of the PSA, he examined me and he said – you've got an enlarged prostate and that's how it got referred" (P13, 10-12).

"The doctor suggested I have a test, a PSA test and they found my PSA was up, up to about four or five I think it was. So I went and saw the specialist" (P14, 8-10).

In one case, the patient had family members with a history of PCa which led him to screening:

"My father had prostate cancer…….and my uncle got it, prostate cancer, and they are both dead. So that's when I decided to go to the doctor and say – look – what about prostate cancer checks? That's when I was diagnosed and it all started" (P4, 9-13; 32-33).

Many of the interviewees articulated a degree of surprise at being diagnosed with a confirmed cancer but in the majority of cases their response to their diagnosis was acceptance and in many cases humour:

"The GP gave me some information, I forget what it was now, but the gist was that the chance of dying from this within the next 10 years was pretty slim. And my attitude was very much – that's okay, I won't book anything after 2022!" (P1, 28-31).

7.4.4. Theme 1: "The safety net has a hole in it" – problems of living with prostate cancer and being managed with active surveillance.

- **Sub-Theme 1.1: PSA Monitoring Issues**

For many of the interviewees, there was a clear element of mistrust surrounding the accuracy of the PSA test and concern over the frequency with which it was performed. Several spoke in a way which signalled an awareness of the widely reported clinical inaccuracies of PSA scores and concern that their surveillance protocol simply involved the periodic assessment of such an inaccurate clinical marker:

"Bearing in mind what they said about it [PSA tests] not being a very accurate indicator of what's going on – I was concerned to find that – the surveillance was, in fact, just to watch the PSA"(P3, 99-102).

The frequency of PSA monitoring was also a cause of concern to many of the interviewees. To differing degrees, over two thirds described experiencing a degree of distress or concern relating to the manner in which their PSA was being monitored and the frequency of such monitoring.

"The most distressing time has been the not knowing that there is a – a structured program for being monitored – well it is a program every six months since being diagnosed but it isn't good enough. They say that my PSA is remaining the same at the moment but how do they know – I only get monitored every 6-months, and a lot can happen in 6-months." (P5, 112-118; 144-146).

There was a sense of mistrust between the patient and the clinical care team and that it was too easy for the disease to develop and progress without being identified in time. For many this was a cause of real concern. The interviewees described feeling that there was not enough PSA surveillance performed in their AS protocol, that the time between PSA tests was too long and a general consensus that the "safety net has a hole in it" prevailed:

"Extending blood tests to 6-months makes you feel like the safety net has a hole in it" (P4, 178).

Tied into the issue of PSA monitoring was the broader issue of disease progression and the fear that extending the PSA surveillance period from 3-months to 6-months meant there was an increased risk of unchecked disease spread. Interviewees' accounts indicated a struggle to accept the concept of simply waiting for something to happen:

"I think there should be more support with this, not to wait and then, all of a sudden, I go up there and the consultant says to me – well, sorry, it's gone in your bones. And what can we do now?" (P7, 166-168).

However, whilst the perceived lack of routine PSA monitoring, and the fear of unchecked disease progression that accompanied it, was a cause of concern for many, it appeared that adequate information provision could in some cases help to alleviate such concerns. Several of the interviewees had had the indolent nature of their diagnosis clearly explained to them by their clinical care team and put into perspective. This in turn helped them to understand the localised, non-aggressive nature of their condition. Such men were much more comfortable with the concept of 6-monthly PSA tests:

"I think the major thing he [the consultant] told me is that – even though I've got it [PCa], he put it in perspective and that, I think, is a major thing, it's not going to grow and kill you quickly. When you know that you are happy to just keep an eye on it every six months" (P6, 107-110).

In contrast, the men who did not receive this kind of insight wanted it and believed that receiving it would have allowed them to cope better with the perceived lack of PSA monitoring:

"I do think – there could be a better way of presenting it; something that would give people confidence in the fact that – yes, we're only going to monitor to you every six months , here's why - because it is important to know about that" (P5, 135-137).

Interviewee responses to the issue of PSA monitoring also highlighted a clear distinction between the "active patients" who were willing to take control of their condition and more "passive patients" who put their faith in the medical professionals caring for them. Whereas several of the interviewees articulated that it was necessary for them to trust their doctors to

act appropriately on their biannual PSA tests, others believed that it was up to them to self-monitor their condition between PSA tests:

"The way I see it is that – if I feel that there has been some significant deterioration in my condition then I would think, well – you know –I'd better go and see my GP and say, look, I've had this problem, it's getting worse and maybe I ought to go and have another PSA check done." (P18, 191-198).

Whilst the length of time between PSA tests was a cause of concern, so was the time immediately before and after the PSA test. Several of the interviewees stated that they felt anxious around the time of their routine PSA tests.

"Yes, waiting on the [PSA] results is the worst because you know that something is wrong, because that is why they send you there – it makes you very anxious" (P13, 188-189).

This is a widely document response within the related research which has been labelled "PSA-itis" (Pickles et al., 2007). It was therefore not surprising that in the current cohort of men, over half expressed a degree of concern around this time. An interesting observation to arise around the issue of PSA related anxiety was the discourse that existed between deviant cases who expressed feeling no concern or distress as a result of their PCa and treatment in general and their response to how they felt specifically around the time of the PSA tests. For example, in regards to the psychological and emotional consequences of his general PCa diagnosis, patient 6 stated:

"Oh, it [PCa] hasn't worried me at all, mainly – because as I said – the consultant was direct, told me what I had and then he put it into perspective" (P6, 256-258).

Yet whilst this participant was reassured by the localised, non-aggressive nature of his disease, as explained by his consultant, he still alluded to experiencing anxiety around the time of his routine PSA test:

"My only moment of anxiety is after the nurse had stuck a needle in my arm and you have to wait till Wednesday when you make your phone call for the results" (P6, 289-290).

Thus even in the interviewees who reported experiencing no or limited psychological distress as a result of their diagnosis, the time around the PSA test, and the wait for the subsequent results, raised the threat of potential progression and this was often described as anxiety inducing.

Over the course of the 20 interviews, several deviant cases were identified relating to the interviewees views of PSA testing. These patients described being happy with the concept of PSA monitoring, finding it reassuring and drawing comfort from the fact that their consultant was confident that routine PSA checks were the best way of monitoring their cancer and its progression:

"I think it is a confidence thing. If the consultant is confident that these PSA tests are the best way of keeping an eye on things, this kind of gives you confidence doesn't it, you feel reassured that this is the best way of doing things, you know – he's the expert after all (P8, 45-49).

Interestingly, these interviewees were receiving 3-monthly PSA checks, rather than the standard 6-monthly checks. This increase in surveillance may be partly responsible for their positivity towards PSA monitoring in the belief that reducing the time lag between clinical tests also reduced the chances of disease progression going unnoticed.

- **Sub-Theme 1.2: Active Surveillance**

Information sharing and communication about what AS is and what it would entail appeared to be an area of concern and frustration. Most of the interviewees had strong views on this issue and felt it was something that had to be improved upon. Many suggested improved communication in the consultation process to ensure that patients leave the hospital knowing why AS was suitable for them, what it would entail and how they would be monitored. Currently these were issues that were not being adequately met:

"Well if they'd had said what AS is then perhaps I might have understood it better – they just said we will keep an eye on it every 6 months. You know – keep an eye on it every six months could mean a blood test, could mean just go up there and speak to a consultant or it could mean another biopsy. You know, I was in the dark with that" (P13; 83-88).

This sense of unease regarding the rationale for, and processes involved in the use of AS, prevailed across most of the twenty interviews. The interviewees' views on AS were that it just did not seem an adequate treatment approach for dealing with a condition as "big"as cancer. They also described not being able to reconcile the fact that they had cancer but were being told that they have nothing to worry about and that nothing was going to be done; this appeared to be experienced as an impossible paradox.

"I personally have a friend that's died from PCa and when you are told – well yes – you've got it, but it's not important, it's – it's nothing to worry about. Well if something can be done, prior to it becoming severe, well why isn't it being done" (P5, 98-102).

The interviewees expressing negative appraisals of AS also provided an interesting contrast to those deviant cases who held positive views of AS. It seems that in some cases, AS was viewed as intuitively "good" as it signalled that their cancer was not serious enough to warrant intervention and that through AS they were able to avoid the debilitating physical side effects of radical treatment:

"Yes, I was quite happy [with AS] - because a friend of mine had radiotherapy for it [PCa], you see, and it upset their system and all that sort of stuff and I thought, oh well, it is slow-growing, I'll – I'm quite happy if they keep an eye on it, you know" (P14, 48-50).

Yet for others, not doing anything was construed as anxiety inducing and it carried with it a risk of chronic uncertainty and fear that the cancer may develop and progress unchecked.

"I had done a lot of reading and certainly a lot of the literature, especially from America where they are very keen on surgery, active surveillance is – looked on as a recipe for disaster. By the time you find there's something gone wrong, there's very little that can be done" (P19, 93-97).

- **Sub-Theme 1.3: General Emotional and Psychological Distress**

A strong degree of consistency regarding the degree and types of general distress experienced by the interviewees prevailed. Many were experiencing either depression, anxiety or both. A degree of introspection was also evident with the interviewees stating how a diagnosis of PCa could raise difficult issues relating to one's mortality which in turn could trigger serious

reflection about the past, their life's achievements and failures. For some this resulted in low mood and feelings of depression:

"What I've found is that you sort of think about other things in your life; if you are sort of told that your life is going to come to an end, you sort of think about other things in your life and you become a bit depressed….from what you've done and what you've not done" (P1, 42-44).

Irrespective of the type and degree of concern identified, the majority of the interviewees stated that the period immediately after diagnosis, and the subsequent 6-12 months following it, were the times that caused the most emotional upheaval. This suggests that for AS patients, the need for emotional/psychological support may be most needed in the first year post diagnosis:

"The 6-12 months post diagnosis were a bit tricky because when you get the diagnosis, you get put through a routine, which is on the sort of shock horror end of things and pretty scary" (P11, 29-31).

Two men stated that distress increased over time whilst others found the time leading up to and immediately after PCa biopsies to be the most distress inducing:

"Probably, probably just before the biopsy, I'd say that was the most distressing time" (P6, 159).

In contrast, several of the interviewees articulated that they had not experienced any distress or concern whatsoever over the course of their illness. It is important to note that the majority of these deviant cases were not experiencing any physical side effects and the slow growing localised nature of their cancer had been explained to them in such a way as to quell any concerns.

"The way it was explained to me – you know – I obviously knew that I had something wrong with the prostate and when he said to me – he said, look, I don't suppose anybody's told you he said but you've got this little bit of cancer, he said – don't get alarmed, it's what we call a slow growing thing – and then he explained to me the chances and what percentage of people have it. So you know – it was no worry" (P13, 174-184)

7.4.5. Theme 2: Managing life and survivorship whilst being managed with active surveillance

- **Sub-theme 2.1: Group based support**

When asked, many of the interviewees articulated strong motivation to attend group based interventions as a means of providing them with the opportunity to receive more personalised PCa information, to share thoughts, ideas and information, as a place to have access to clinical experts and to have questions answered. Indeed, interviewees' accounts suggested that it was common for questions to remain unanswered following clinic appointments and nurse led follow ups, usually about their diagnosis and treatment. The enthusiasm for group interventions was construed as an ideal way to address this problem:

"Very often, there are many questions that a person won't – or doesn't feel comfortable – asking their doctor or specialist but in group therapy, more would come out and different questions would be asked and people would have more confidence in asking about their concerns" (P5, 204-208).

During the interviews, the reasons why the interviewees believed group based support to be so beneficial was further probed and the subsequent discussions could be grouped into two distinct categories.

Firstly, a small proportion of the interviewees found value in the concept of group based support as a means of allowing them to compare themselves and their problems with others who were in a similar situation to themselves. They described a belief that this would allow them to learn from others about living and coping with PCa. Furthermore, interviewees' described how new questions and answers were likely to be generated in a group context which would benefit the group as a whole:

"With a group of men, one of them might come up with a question that the others hadn't thought of at the time, you know what I mean and a question which, when it's raised they think – oh yes. I think, yes, I think it could be really useful" (P10, 205-208).

The second and most common reason that the interviewees found benefit in the concept of group based support was as a means of sharing information about PCa, treatment and disease

progression. Across the interviews there was a constant awareness about the potential need for future radical treatment and that this was ever present in their minds. As a result of this the interviewees articulated a need to know more about what this would entail, the associated side effects of radical treatment, when initiation of such treatment becomes advisable and how they would know when they had reached this point. It was also suggested that it would be of benefit to have PCa patients who have gone through radical treatment to come and talk to the group so that the AS patients could receive first-hand knowledge of the "real life" consequences of the radical treatment from men who have been through it:

"Yes I think information during the group session about the treatment, if you need treatment, what treatment – go into the treatment more and tell what happens and what effects it could have and what new treatments are coming in" (P14, 151-158).

Deviant cases were observed however when discussing the use and benefits of a group based support programme, with three of the interviewees articulating potential concerns about group support. These concerned centred primarily on the fact that men may not want to share personal and intimate issues in a group based environment:

"There might be a lot of other people that it would be not something that they want to discuss in public – or not in public, even with another – say – a couple of people, do you know what I mean, whereas they might be happy to talk on a one-to-one basis with an experienced person, but it may not work well for a group" (P1, 438-442).

One of the interviewees also stated that they didn't think group based support was a good idea simply because they didn't like the idea of listening to other people's problems.

"It [group support] wouldn't be sort of like my choice. As far as I'm concerned, my problem is my problem and everyone else's is there's and, you know, I wouldn't want to sort of like listen to other people's problems" (P13, 275-277).

- **Sub-theme 2.2: Need for additional information provision**

Issues relating to information provision represented the largest sub-theme generated during the data-analysis process and one that transcended and impacted upon all three overarching

themes. Across the twenty interviews it appeared that information was in most cases provided to the patients through leaflets that they were given or that they had picked up during clinic appointments. Some were happy with the provision of information they received but for the majority there was a distinct lack of information provided to them.

P19, 116-120: "I think it probably would have helped I think, if there had been something that had explained everything a bit more. I think it would have been better I think, had I been given, say, a CD or pamphlet explaining all the various options".

In the majority of cases, the interviewees articulated that their need for additional information was to help them better manage and lower any concerns they held about their diagnosis and treatment. It seemed that receiving information about the slow growing indolent nature of their PCa acted as an effective coping method to allow them to better manage any concern or distress they were experiencing. As already discussed in Sub-Theme 2.1 above, in several cases interviewees who received such information appeared to be much better placed to cope with the stresses associated with waiting for their 6-monthly PSA tests:

"I think the major thing he told me is that – even though I've got it, he put it in perspective and that, I think, is a major thing, it's not going to grow and kill you quickly. When you know that you are happy to just keep an eye on it every six months" (P6, 107-110).

Furthermore, rather than simply helping to lower concern, information provision was seen as an important method of allowing the interviewees to increase their health literacy related to PCa and its treatment. Over half of the interviewees articulated a strong need for more information about the different forms of treatment for PCa, the side effects associated with them and when such treatments should be initiated. A strong sense of mental preparation prevailed in relation to the issue of future treatment and receiving adequate information was the means by which they could prepare themselves fully for what was to come should radical treatment be needed:

"It would be very useful to know what the next treatment stage is likely to be, after the one you are having, so that I think you can sort of get your mind ready for it" (P2, 423-425).

This need to be both aware and mentally prepared for potential future radical treatment may have been a means of generating a degree of control over the situation regarding their health

status. This was a sentiment echoed strongly when discussing issues relating to PSA monitoring during which the interviewees often struggled with the concept of doing nothing and simply waiting for their cancer to progress. It may have been due to this need to regain a degree of control over the situation that most of the interviewees wanted additional information to help them better self-monitor and self-manage their condition. This included a desire to better understand which symptoms to look out for that might suggest disease progression along with receiving information about how they could help themselves improve their prognosis:

"Is there any way of self-monitoring in between the – the testing period of every six months?" (P5, 128-129).

"What can you do, actively, yourself. Are you on a high risk diet; do you take this or that? This may help" (P4, 390-392).

"What's out there, you know, apart from anything else – is there anything else out there to help the situation" (P7, 369-370).

A common complaint was that the interviewees felt under informed about their diagnosis and treatment. Crucially, in several cases this lack of information appeared to have negative impacts upon treatment decision making and regret that radical intervention was not chosen and initiated sooner:

"I feel under informed and I would very much liked to have been better informed over the last 6 years – I would have started hormone treatment sooner" (P2, 437)

This suggested that a lack of informational support about localised PCa and its treatment can have a direct and possibly negative impact upon clinical decision making. Yet somewhat ironically, it also seemed that receiving additional information, if it was not fully and clearly explained, could also lead to patient concern and anxiety:

"You know, he (the doctor) said something like you haven't got cancer as such, they are just pre-cancerous cells. So you are sent home wondering have you got cancer or not. You need clear and concise information about what you have got, not ambiguity which for me was more concerning than the actually diagnosis, or lack of shall I say." (*P18, 185-187).*

Thus whilst in some instances the interviewees did receive more detailed explanations about their condition, and it's very localised histology, it seems that unless this was discussed and understood fully by the patient, it has little effect in lowering concern but could, in some instances, exacerbate it. It would therefore appear that a very fine line exists between the emotional distress caused by a lack of informational support and too much information that is not fully and completely grasped and understood by the patient. Similarly, over half of the interviewees articulated a concern that due to a lack of information, they were at risk of carrying on negative lifestyle habits that could be having a detrimental effect upon their PCa and its progression:

"There is such a lack of information that you just carry on as normal doing things that may be bad for you like eating red meat" (P4, 776-780).

- **Sub-Theme 2.3: Supporting emotional/psychological health and wellbeing**

The majority of the interviewees communicated a need for, and benefit in, having an emotional and psychological component to the group intervention. The majority of the interviewees also stated that they would be keen to learn some specific stress management techniques:

"Most people get distressed, I think, through becoming slightly obsessional about a particular thing and find it very hard to move outside of it. So it's a question of focusing of thoughts – or de-focusing of thoughts – is the fundamental thing and there's various ways in which you can attempt to do that. I mean there's the – the sort of concentration on breathing….and those sorts of things – which would be very useful" (P11, 289-295).

Whilst the interviewees appeared keen on the idea of learning techniques that would allow them to better manage their distress, the structure and format of the support and the way it was offered and delivered was important. The general consensus to emerge from this sub-theme was the importance of creating and designing the support intervention in a way that would resonate and appeal specifically to men. Many traditional masculine views came up from within this sub-theme, all of which strongly suggested that if these kinds of psychological/emotional interventions are to be offered, taken up and be effective, they must be presented and delivered in a way that will make men feel comfortable:

"If it's [the group intervention] a bit wishy-washy - and new wave, earth-type thing, you know, let's go and look at the Ley Lines, I think – some men, it would put off. I think I'd be sat there going – ohhh and looking at my watch, but if someone got up – one of the guys said – look this breathing exercise worked for me, you know, come on – give it a go. We're going to do some breathing exercises, let's see if we can clear our heads here, at this meeting – get ourselves sorted. Because it could be more like – a football huddle, wouldn't it? (P4, 694-700).

Whilst the majority of interviewees articulated a desire for additional emotional support, many had developed their own coping strategies to allow them to deal with both their diagnosis and management with AS. These coping strategies varied greatly. Some men were extremely accepting of their condition, stating that there is nothing you can do about it; once your time is up it is up.

"I always believe that – what's life is life – and that's the end of it, do you know what I mean. One day it will end and I'll enjoy it until that point then – so what, you know" (P1, 594-596).

Other men aimed to put their PCa at the back of their mind and ignore it, which in many cases was made possible by their knowledge of the slow growing, non-threatening nature of their PCa. Other men developed a much more hard lined approach, comparing their response to PCa as a battle which they were determined to win:

"I sort of came to the conclusion that right – either this thing is going to beat me or I am going to beat it. So I decided on the latter option basically and so far that seems to have had a fairly satisfactory outcome" (P18, 57-60).

Sub-Theme 324: The structure and design of group based support interventions

- **Running of the Group**

Importance and role of the clinical nurse in the group sessions

Many of the interviewees held strong beliefs about the importance of having a clinical PCa nurse to run or be a part of the group intervention. The interviewees stated that their presence was a "must" rather than an optional extra to ensure that they would have access to top quality clinical advice during the group sessions:

"I think what people on surveillance want to know is – if I have to have treatment then what kind of treatment is on offer and what would be best for me…and the nurses can tell us that, so it is crucial they come along to the sessions I think" (P8, 100-107).

However, it was also pointed out that the character of the nurse would be important; they can't just be clinically good, they also have to be engaging and personable:

"The nurse must have a disposition where they can – they are able to join in and that. I mean, you can't just – it doesn't matter how clinically good you are as a nurse, if she hasn't got that side to her…it isn't going to work at that level….they have to have natural charm" (P4, 569-573).

Timing, duration and size of group support interventions

Whilst the majority of interviewees held similar views on the importance of having a PCa nurse involved in the running of the group, their views on when the best time to have access to the group based support varied widely. However, the general consensus from the majority of the interviewees was that group support should not be offered immediately after diagnosis because patients are likely to be too "stunned" and shocked at this early point to benefit from the sessions, but that it should be offered within the first 6-12 months of being diagnosed:

"I wouldn't want access to an intervention immediately because I think you are a bit sort of stunned by it [PCa diagnosis]. Again, perhaps four-five weeks, so it's given you a bit of time to sort of accept it and settle down with it a bit. I think if it came too early, it would be too much of – too much of a shock and you might find it difficult to absorb, whereas with a little bit longer, you know, say four or five weeks, that extra time will probably make you more open to listen and really absorb it" (P10, 371-376).

Interviewee responses to the issue of group sizes were highly consistent, with all of the men stating that an optimal group size should be between 6-12 patients, which is very much in keeping with the group sizes observed in other cancer support group research. Several men articulated why they believed this group size to be optimal:

"I think probably a smaller number, I think possibly if you had too many it might become – more like a sort of lecture than a sort of discussion group – an actual number, now – oh … perhaps half a dozen to around 10, or something like that." (P10, 332-334)

Interviewee responses to how long each group session should last were also relatively consistent. The general consensus was that the sessions should last for between 30-60 minutes, with several men stating that once the sessions go over one hour, it is likely that people would begin to get bored. One man thought the sessions should be two hours in length but this was an isolated view. Another man also stated that it would be very important to schedule in 30 minutes at the end of the formal session for people to chat informally and maybe to have private access to the nurse:

"Then a little – say - 30 minutes at the end where you just talk to each other. So you can go up – if you don't want to ask the question of somebody else, you could go up and say – look mate, I don't like to ask in front of everybody else, but what about your sex life – honestly? How does it affect that? Do you see what I mean? There's always somebody who is not going to ask the question out loud and they are going to want to – a little one to one, perhaps – an opportunity" (P4, 519-525).

"Yes, one hour per session: if it gets too long people get bored. One hour and then - they won't have asked all the questions and will want to come next week or next month to find more out" (P5, 300-3020.

The opinions of the interviewees regarding how many group based sessions should be offered and at what time intervals varied substantially. The majority of men stated that it would be best to offer between 3-5 sessions, with anything more than that becoming too much:

"I would have thought – probably somewhere between two and four sessions, but I wouldn't – more than four would probably be a bit too much and whether you could get everything done in two, I don't know." (P19, 306-308).

An interesting point to arise during the interviews centred on the actual process and practicalities of running the group and how to make it as "male friendly" as possible. It was important to the majority of interviewees that the sessions be presented as casually as possible to allow men to open up and ask questions. They also thought it was important to ensure that the information shared during the sessions was broken down into clear steps to

avoid information overload. It was also suggested that having a slide presentation would help to show what was going on:

"I would say that a slide presentation to show what is going to happen would be really important" (P4, 371).

"I think, obviously, it needs to be very casual and allow people to sort of ask questions and maybe open up slightly - I would say – without a shadow of a doubt – it has to be informal, relaxed, cup of tea" (P6, 374-379).

Sub-Theme 2.5: The role of the internet

The majority of interviewees communicated strong positive views on the benefits of having a PCa/AS specific website available to them. Most of the participants had used the internet to search for PCa specific information and several of the interviewees stated that having access to a website that is being designed and built via a project that involves Southampton Hospital makes the whole concept more helpful and credible.

"Yes, I think that [the PCa specific website] would be very helpful, especially if it was actually from the hospital itself, not just a general blog that some geezer's wrote on there. Yes, yes and if that's coming from the hospital, you know, under the urology department – you know – you'll know it's bona fide findings" (P13, 434-435, 454-455).

When asked to elaborate on why they though a PCa/AS specific website would be so helpful, the reasons could be categorised in two ways. Firstly was the belief that by having access to educational, informational and emotional online support, they would be better able to self-manage their condition and be reassured by the information they had access to.

"If the [PCa] information was available on the web, then that reassures people. So things like frequently asked questions, situations to look for, advice on what you can do to help it [PCa]. As I said to you, advice about my diet, changes that I ought to try and do, things of that nature. And so, you know, those sorts of things. That would be very useful on the website" (P1, 676-683).

Secondly was the belief that the information available on the website would work very well in tandem with the group session by helping men to cope better with the information and topics discussed during the group sessions and by ensuring that men who cannot make the group sessions still have access to the same information, via the website:

"It's [the PCa website] very efficient too, because once it's on the web; I mean– probably about 80% of the people can actually find it, especially if you tell them it's there, they can even go to the local library, they could look it up, so it would simplify enormously – and probably might cope with the intellectual side of the problem actually – alongside these group sessions where you can go and ask questions – it would be a great help" (P11, 394-398).

The majority of the interviewees were very clear on the type of information they would like to see on the website. Such information tended to fall into four distinct categories that included 1) a frequently asked question section, 2) information on lifestyle, diet, exercise and other self-care approaches, 3) information on PCa; progression, treatment, symptoms and clinical management and 4) information about AS such as survival statistics associated with AS, the clinical side effects of AS, how the Gleason score and PSA score interact and the influence this has on AS and any subsequent radical treatment after AS:

"Well let's say you could log on a program and there was the frequently asked questions on there and you can run through them, do know what I mean, that would be useful to know" (P1, 375-377)

During the interview process it was important to understand how many of the participants currently used the internet. Interestingly, the majority did.

"Well I have to say, I think that problem [of older people using the internet] is overstated. One of my activities is playing bridge and – I look after a couple of websites for that and people are always saying, oh, what about people who don't have access to the internet? You find, when you actually get down to it, you find they all have and – this thing about older people not having access to the internet, is – is actually … a mistake, in my experience" (P16, 260-266).

7.5. Discussion

7.5.1. Key Findings

The current investigation has provided an important insight into men's experiences of being diagnosed with PCa and managed with AS and how best to support them during this process. It is hoped that this information will enable the design of interventions that will aim to support AS patients to allow them to better cope and manage their distress.

A key finding of the current investigation was that AS patients report experiencing a relatively high level of psychological and emotional distress, concern and anxiety around their management with AS. This distress was largely attributed to fears of unchecked disease progression and a perceived lack of information about their management with AS and support from the patient's clinical care team. This appeared to heighten the uncertainly, anxiety and distress they were experiencing. The results from Chapter 4 of the current PhD provided a clear quantification of the high levels of depression and anxiety experienced by a large cohort of AS patients within the UK. The results of the current investigation provide a rich qualitative account of what factors may be contributing to this distress.

The findings also revealed that AS patients subscribe to and acknowledge a need for additional support, education and information to allow them to more readily manage their concerns and distress. In particular, they appeared to like the concept of group based support, with the majority of patients reporting a belief that they would like access to such support and would attend sessions if they were available to them. Currently, the research base into male cancer patients' willingness to recruit into and adhere to group based support programmes is equivocal and conflicting (Oliffe et al., 2008; Kronenwetter et al., 2005). The findings of the current investigation however suggest that AS patients acknowledge a need for and a willingness to take part in group support programmes to help them manage the uncertainty and distress that is commonly experienced by this patient group (Burnet et al., 2007; Hedestig, Sandman & Widmark, 2003).

However, it is important to note that hypothetically talking about and discussing the use of group support, and their willingness to take part in it, during an interview is likely to be considerably easier than it is to actually engage in such support in the real life setting. Therefore just because the majority of interviewees in this investigation were positive about the use of group support during the interviews does not mean that this would translate to an

actual willingness to recruit into and adhere to such interventions when offered to them in the real world setting.

The final key finding was that AS patients articulated extremely positive views about internet based support programmes. Almost all of the 20 interviewees believed that web based support was an absolutely essential service that would allow them to have access to evidence based information and education about AS, and all of the issues surrounding it, in the comfort and convenience of their own home. This finding is interesting; it has been suggested that delivering web based support programmes to elderly medical patients is challenging based upon the assumption that patients in this age bracket are less confident with and thus less likely to utilise web based support services than their younger counterparts (Cotton & Gupta, 2004). My findings suggest that in the current cohort of patients, this was not the case.

However, it was again important to note that the positive views articulated by the interviewees regarding the concept of an AS specific web based support intervention were hypothetical. This positivity may not transfer to the real world setting if the interviewees were actually required to utilise this form of support. The only way that it will be possible to determine whether or not this would be the case is to pilot such an intervention.

7.5.2. Limitations and Strengths

Whilst the findings of the current investigation provide a novel insight into the psychological and emotional sequelae of AS, important limitations exist that must be accounted for when addressing the relevance of the findings.

Firstly, the study utilised a cross-sectional methodology. By definition this approach was unable to assess how the psychological, informational and educational needs and wants of this patient group may have varied over time. The clinical management of PCa with AS involves a detailed and specific methodology with a clearly defined timeline of tests that commonly include PSA testing, biopsies and MRI imaging. It is well documented that anxiety and distress increase around the time of such tests (Lofters et al., 2002; Pickles et al., 2007). For most men, PSA tests and MRI imaging occur once every 6-months. Unfortunately the restrictions placed onto this investigation by Research Ethics Committee meant that it was not possible for me to access confidential clinical information about where each of the interviewees were on their monitoring cycle. If I captured and interviewed patients equidistant between their last and next clinical surveillance test, it is possible that they would be far less anxious and distressed than in the weeks immediately before and after such a test. This reduced level of psychological

distress may have “reduced” in the patients mind their need for additional information and support, a need that may be far greater around the time of a clinical test such as a MRI scan or a PSA test.

As a retrospective investigation, I was also asking AS patients to recount their thoughts and experiences of AS when they were first placed onto their surveillance protocol. It was possible that in many cases this would have been many months or years ago. This time lag may have had some impact upon how the patients recalled their experiences at that time. To address this would require a far longer recruitment period than a PhD would allow and would involve utilising a prospective, longitudinal methodology with patients who have been recently placed onto AS. This would allow for a more accurate assessment of patient experiences of AS at the time of being placed onto this management pathway rather than relying on retrospective accounts.

Lastly, the AS patients interviewed as part of the current investigation were extremely open and willing to discuss the psychological and emotional side effects of being managed with AS. This willingness to do so appears to be uncommon. Research has highlighted that elderly male medical patients, including PCa patients, are traditionally far less willing to discuss issues concerning their emotional and psychological wellbeing (Moynihan, 2002; Chapple & Ziebland, 2002). It may be that the patients who agreed to take part in the current investigation were a self-selecting sample who were happy and comfortable with the concept of discussing personal and emotional thoughts and experiences. It may therefore be that the participating men were encouraging and supportive of the support interventions discussed during the interview (i.e. group support and internet support) due to their inherent affinity for talking based group support approaches and their willingness to discuss and address such issues. Such characteristic may not be reflective of the wider AS community.

As with all qualitative studies it was not possible to claim to know how the reports generated through this investigation compare to those likely to be generated by other non-responders or others not approached. The interviews did however sensitise me to some important issues that are likely to be relevant to and resonate with other men being managed with AS. Indeed some of the findings resonate with the existing literature on related topics which lends credibility to the generated findings. Furthermore, the relatively high response rate observed (62.8%) and the consistency in themes in the interviews lend confidence to my findings.

An important strength of the current study is the novel area of research that it addresses. In recent years there has been an increase in the volume of qualitative research into and around

treatment with AS (Davidson & Goldenberg, 2011; Volk et al., 2013). The majority of this research has focused very specifically on the treatment decision making process by assessing what factors influence a patient with localised PCa to opt for and remain on AS (Volk et al., 2013; Davidson et al., 2009). Such research is important and has obvious value. However, it does very little to further our knowledge of how we can actually support AS patients to better cope and manage with the uncertainty of AS and so reduce the number of men transferring to clinically unnecessary radical intervention. Thus, a very important strength of the current investigation was that it is one of the first of its kind to specifically explore the supportive needs of a cohort of AS patients within the UK to help establish how to design an intervention that can effectively address these needs from the patient's perspective.

The fact that saturation was reached early on in the interview process also represents another important strength of the investigation. Saturation refers to the point when no new or additional themes or insights are generated from each subsequent interview. Reaching saturation suggests a high degree of consistency across the data collection process and increases the transferability of the findings. That saturation was reached by interview number 15/16 (out of 20) would suggest that the points being raised by the interviewees in regards to their supportive needs and how we can best manage them provides a trustworthy and credible account of what a range of AS patients need and want out of a supportive intervention. This enhances the possibility that any subsequent intervention that is generated out of the findings of the current investigation will be acceptable to AS patients.

7.5.3. Overview of the key findings in relation to the previously conducted research

- **Problems of living with AS**

One of the key aims of the investigation was to provide an insight into the types of problems and concerns experienced by PCa patients being managed with AS in the UK. Sociological research shows that cancer is often a dreaded disease in the public mind (Klotz, 2013) and the receipt of a positive diagnosis is laden with stress, anxiety, fear and depression (Hulbert-Williams et al., 2012; Gil et al., 2012). It is likely that these concerns are further exacerbated when one is diagnosed and told that no radical, curative treatment is required but that the disease is simply to be monitored, as is the situation faced by men who are placed onto an AS protocol. It is the uncertainty and fear of living with an "untreated" cancer that is believed to be one of the predominant causes of psychological distress in AS patients (Latini et al., 2007;

Hedestig, Sandman & Widmark, 2003). The qualitative findings of the current investigation suggest that this was the case for some of the men interviewed in this study.

To varying degrees, almost all of the interviewees articulated a degree of concern, anxiety, uncertainty and distress around their management with AS. One of the predominant reasons for this was a perceived lack of adequate information and explanation about what AS was, what it entailed and how and why it was a suitable, safe and clinically viable option for them. In one of the few previously conducted qualitative investigations into the psychological burden of AS, Chapple et al., (2002) revealed similar findings, identifying that across 25 AS patients, a predominant concern was a lack of information about and support from their treating clinician about AS and what it entailed.

Within the field of PCa, lower levels of information provision regarding a patient's chosen treatment option has been shown to be significantly correlated with higher levels of psychological distress (Gray et al., 1999). Indeed, recent evidence has shown that patients with low risk PCa are significantly more likely to opt for and remain on AS when they have a multidisciplinary team (MDT) consultation than when having a 1:1 consultation with an individual clinician (Aizer et al., 2012). This is primarily due to the additional information and support, and the increase in patient-physician trust, that is believed to stem from the former approach. Such findings, and those observed in the current investigation, would strongly suggest that ensuring that AS patients fully understand the concept of AS and why it can be a safe and suitable treatment approach for them may go a long way to ensuring that patients feel comfortable with AS which in turn may help them to better cope with any feelings of uncertainty and anxiety.

This would seem additionally plausible given that the majority of the interviewees reported that they had received very little information and reported a high level of ambiguity about their prognosis and treatment. This lack of information was often deemed to be more distressing and concerning than the actual diagnosis itself. Hack et al., (2012) showed in a large randomised controlled trial that PCa patients who received an audio-tape of their initial treatment consultation to listen to in their own time reported receiving far more information and far more satisfaction with their treatment choices than patients who did not receive an audio recording of their consultation, even though the information provided in each was the same. This suggests that treatment information provided verbally during a consultation may on its own be insufficient to address the informational needs of AS patients and that additional modalities of information provision may be required.

Whilst over half of the men interviewed articulated a belief that they had not received adequate information about AS, this may have been due to the patients not fully taking in all of the information provided to them by their treating clinician rather that an actual absence of information. Given that patients often find it hard to recall everything articulated verbally in a consultation (Hack et al., 2012), it is likely that to meet this informational demand, hard copy or electronic information provision will be required to supplement that provided verbally during the consultation process. For patients being managed with AS who face such uncertainty around their diagnosis and treatment (Hedestig, Sandman & Widmark, 2003), this may be an issue of key focus when trying to understand how best support this patient group.

However, the results of the current investigation also suggest that the provision and use of information as a means of helping AS patients better cope and manage with uncertainty and anxiety is not a straight forward solution. In several patients, having the indolent and low risk nature of their PCa fully explained to them by their treating physician allowed them to rationalise and accept the use of AS; they were able to reconcile the passivity of their treatment with the equally passive nature of their disease. Identical findings have been observed in the qualitative research conducted by Oliffe et al., (2009) who observed that when the extremely low risk nature of AS managed PCa was fully, clearly and repeatedly explained to patients, they experienced a marked reduction in distress.

Yet my findings also suggest that in some instances being provided with too much information can be counterproductive and induce further concern if such information is vague, unclear or ambiguous. For example, patient 18 in the current investigation stated that his treating physician tried to put the indolent nature of his PCa into context by stating that he did not have cancer as such, but just pre-cancerous cells. Presumably this was done to reassure the patient that radical intervention was not required and the AS was an appropriate and suitable approach to take. Unfortunately, the provision of this type of ambiguous information was perceived and experienced as distressing by the patient rather than comforting as he was left unclear about whether or not he actually had cancer and what this ambiguity around his diagnosis and management with AS meant for the future.

There is currently a growing body of support for a change in terminology amongst urologists to describe Gleason 6 PCa not as cancer but as IDLE lesions (indolent lesions of epithelial origin; Esserman, Shieh & Thompson, 2009). It is speculated that by removing the word “cancer” from the diagnosis in this way, AS patients will experience less anxiety and concern and thus less desire to transfer and opt for clinically unnecessary radical treatment (Klotz, 2013; Esserman,

Shieh & Thompson, 2009). The risk of doing so however is that if further information is extracted from the physician by the patient asking questions such as "*so I don't have cancer?*" the ambiguity that this could generate may induce additional concern and mistrust within the patient regarding his diagnosis, treatment and confidence in his clinical care team. Therefore a crucial finding to come out of the current investigation relating to our understanding of the problems and concerns of men on AS is that information provision may have a key role to play in allowing patients to better understand, rationalise and accept AS but to do so this information must be tailored, accurate, honest and delivered in context in a clear and unambiguous way so that it is rendered understandable by the patient and their family.

- **Managing survivorship whilst on AS**

The key aim of this investigation was to develop a greater understanding of the types of interventional support that AS patients would be willing to recruit into and adhere with to allow them to better manage the uncertainty and anxiety associated with AS and so reduce the number transferring to clinically unnecessary radical intervention. The findings suggest that group based support may act as an effective means of doing so. The majority of patients articulated a strong and positive response to the concept of AS specific group support, for three key reasons.

Firstly it was believed that group support would be helpful as a means of allowing patients to initiate contact with, and receive mutual support from, other men who were in a similar situation to themselves. Developing peer support in this way was seen as a positive component of group support and one that would allow patients to both support and learn from the other men in their group.

Similar findings were observed by Kronenwetter et al., (2005) in men being managed with watchful waiting (WW). It was shown that one of the most substantial benefits obtained by men taking part in a group based PCa lifestyle intervention was not the information they received about lifestyle alteration but the mutual support, closeness and feeling of belonging that developed amongst the patients during the programme. This closeness led to substantial increases in hope, optimism and positivity.

The majority of PCa patients attending support groups report a moderate to high degree of emotional and psychological dysfunction (Pickles et al., 2007). It has been shown that a "stiff upper lip" mentality often prevails amongst PCa patients when they are fulfilling their societal role as husband, father, employer or employee (Oliffe et al., 2009). This "stiff upper lip"

approach may add to and exacerbate the distress they are experiencing. Yet it appears that when surrounded by other men with a similar diagnosis in the safety and confidentiality of a support group, PCa patients are able to let go of this stereotype and open up to, learn from and in turn support their peers. This appears to have a largely cathartic effect. Based on these findings it would appear important that any intervention aiming to education and empower patients to remain on AS rather than opt for radical intervention will need a component of group support.

The second and predominant reason that patients found value in the concept of group support was as a means of gaining access to much more detailed and specific information about PCa, AS, disease progression, radical treatment and self-care. As alluded to, a lack of and ambiguous information about diagnosis and treatment was one of the most common causes of distress in the men interviewed in the current investigation. It was therefore unsurprising that an informational/educational group support programme was so well received by the participants as it could provide them with an ideal means of receiving the kind of tailored and individualised information they required. This was particularly true when the concept of having a PCa nurse specialist co-run the group was discussed; having a clinical expert available in this way appeared to reassure the interviewees that the information they would receive during the groups would be trustworthy. However, it is important to note that even in a small group setting, the extent to which the provided information could be tailored to individual patient scenarios is limited.

Each AS patient's clinical condition and thus information needs are unique (Lintz, Moynihan & Steginga, 2003). During busy clinics, clinicians and nurse specialists do not always have the time and resources to answer and address each patient's questions, concerns and fears (Cockle-Hearne & Faithful, 2010; Brown, Koch & Web, 2000). Because PCa patients informational needs vary greatly (Feldman-Stewart et al., 2004), it is highly unlikely that a standardised information package or booklet will be able to address such heterogeneity (Pickles et al., 2007; Feldman-Stewart et al., 2004). AS specific, nurse led support groups may therefore offer an extremely effective means of providing AS patients with the relatively personalised disease specific information they require. If a lack of information is a contributing factor for psychological distress, as this and other investigations have shown (Hedestig, Sandman & Widmark, 2003; Oliffe et al., 2009), then information focused support groups may provide an effective means of equipping patients with the information they require and so help lower distress and anxiety.

Furthermore, it has been observed that it is the "doing nothing" aspect of AS that patient's find the hardest to accept (Chapple et al., 2002). Managing cancer by doing nothing has been shown to represent an impossible paradox, both in the current investigation and in others (Oliffe et al., 2009; Chapple et al., 2002). Relatively recent qualitative investigations have shown that AS patients have an inherent desire to actively "do something" to combat this passivity (Oliffe et al., 2009). Attending a group support programme may help address this issue by allowing patients to combat the "not doing anything" by actively "doing something". A perceived lack of control has been linked to lower levels of health related quality of life in cancer patients and higher prevalences of distress (Kazer et al., 2011). Helping AS patients feel that they can impart a degree of control over their situation by proactively engaging and choosing to take part in group support may have positive impacts upon increasing feelings of empowerment and thereby lowering distress.

Finally, if those working within the field of PCa are to devise effective interventions to help support patients to remain on AS, it would appear fundamental that the intervention shares with patients specific tools and techniques that will allow them to more effectively manage any existing stress, anxiety and concern. Across the interviews conducted as part of this investigation, the majority of patients articulated a need to have stress management techniques taught to them as a component of any group intervention. Furthermore, the patients were open to the concept of breath and mindfulness based exercises and were willing to engage in and utilise such techniques if they were effective at helping them better manage their distress. Indeed, several patients made direct references to mindfulness and meditation, suggesting that such concepts were already known to these participants.

Health psychology theory suggests that uncertainty within the health care setting only becomes undesirable when the patient believes that the outcomes associated with such uncertainty will be negative (Mishel, 1990). Whether a patient views health related uncertainty as positive or negative depends heavily upon the resources they have available to help them cope and manage such uncertainty (Lazurus & Folkman, 1984). If the demands of a situation exceed a patient's ability to cope, psychological distress is likely to ensue.

Sociological evidence suggests that male medical patients are very effective at developing and initiating problem-focused coping strategies (Nicholson, 2000; Kiss & Meryn, 2011). Problem-focused coping strategies involve approaches that effectively remove the source of distress rather than trying to effectively manage the specific causes of the stressor. For example, if an AS patient was experiencing a high degree of anxiety as a result of living with an untreated

cancer, problem-focused coping would involve the transference to and initiation of radical treatment; doing so would remove both the problem (untreated PCa) and the anxiety associated with it.

However, in the absence of problem-focused coping, patients must rely on emotion-focused coping strategies. Emotion-focused coping involves dealing with and managing the emotional concomitants of a stressor itself rather than trying to simply remove it, as is the case with problem-focused coping. If AS patients do not have available to them effective emotion-focused coping techniques to manage anxiety and distress, such as mindfulness based approaches, Cognitive Behavioural Therapy techniques or relaxation and autogenic approaches to name a few, then any distress they are experiencing may develop and progress until the point is reached when the patient has no choice but to implement problem-focused coping strategies by transferring to radical treatment. It is believed that this is one of the primary reasons AS patients with stable localised disease transfer to radical treatment despite the lack of clinical evidence of progression (Pickles et al., 2007). If we are to design interventions that are going to effectively reduce this transference, it will be essential to share with AS patients a variety of effective stress management techniques that will enable them to develop effective emotion-focused coping strategies that will allow them to better manage and live with AS and the uncertainty therein.

Alongside group based support, the findings of the current study also suggest that internet based interventions may act as an effective means of equipping AS patients with additional informational and emotional support. Evidence supports the effectiveness of internet interventions in a variety of clinical settings that include smoking cessation (Shahab & McEwen, 2009; Myung et al., 2009), mental health (Spek et al., 2007; Andersson & Cuijpers, 2009), hand washing (Yardley et al., 2011) and irritable bowel syndrome (Ljotsson et al., 2010) to name a few. By eliminating the costs associated with practitioner and paper based interventions, internet interventions are extremely cost effective to develop, run and maintain (Swartz et al., 2006). They can also help to improve service delivery to patients by providing them with 24-hour access to detailed and personalised disease specific information whilst allowing healthcare professionals to monitor health status.

The majority of the patients interviewed articulated positive views towards the concept of an AS specific internet support intervention. It has been documented that upon receipt of a positive cancer diagnosis, a patient's first response is very often to acquire as much information as possible about their condition, often via the internet (Castleton et al., 2011;

Case, 2012;). The findings of the current investigation suggest that patients being managed with AS experience a distinct lack of information which in many cases forced them to search for information about PCa and AS on their own. One of their concerns about doing so was the sheer volume of information available to them on the internet and not knowing what information to trust and which to reject. One of the common reasons that the concept of an AS specific internet support intervention was so well received in this study was that the knowledge that the intervention was being designed by Southampton University, in conjunction with Southampton General Hospital, meant that the patients knew the content would be safe, evidence based and therefore trustworthy. In this way, an internet intervention would act as a "one stop shop" for PCa and AS information.

The participants in this study also had clear views on the type of information they would like to see on such a website. This included 1) a frequently asked questions section, 2) information on diet, exercise and stress management, 3) a section on PCa and what radical treatments are available should they be required and finally 4) a detailed information section on AS, what it entails and the survival statistics associated with it. Increasing patient health literacy around such issues may provide an effective means of increasing emotion-based coping ability by giving AS patients the information and support to better deal with the uncertainty of AS. Doing so may allow them to better cope with the anxiety and distress associated with AS which in turn may help to lower the number of men transferring to clinically unnecessary radical treatment.

However, an important concern to address when contemplating the use of internet support interventions in this way is the average age of men being managed with AS in the UK. In the related research there is an anecdotal assumption that individuals aged over 65 are less likely to either have access to or be using the internet (Cotton & Gupta, 2004). However, recent research suggests that almost 60% of over 65's in the UK currently use the internet, suggesting that age is not a barrier to usage (Office for National Statistics, 2013). The findings from the current investigation very much support this view. Out of the 20 patients interviewed, 17 currently used the internet on a regular basis and the majority believed that the problem of older men not using the internet was overstated. In light of such findings it would seem that the higher age of men with PCa should not deter researchers from contemplating the use of internet interventions to help manage, inform and support these men. Indeed, there are two large international research projects currently underway into the design and trialling of internet interventions to help post-radical treatment PCa patients better manage the physical and psychological burdens of treatment induced side effects (Wootten et al., 2004; Osei et al.,

2013). This would suggest that the use of internet interventions may have a central role to play in supporting PCa patients across the treatment spectrum.

7.5.4. Way Forward and Conclusion

The current investigation is, to the best of my knowledge, the first of its kind to qualitatively assess the psychological and emotional problems and concerns experienced by a cohort of British men being managed with AS and how best we may be able to manage such issues through the design of an AS specific support intervention.

The findings have revealed that being managed with AS can be a challenging experience and one that, to varying degrees, can place substantial psychological and emotional demands upon a patient. The findings also suggest that the AS patients are very aware of what the underlying causes of their distress are and how, and in what ways, supportive interventions could be designed to help address and remedy such issues. The data generated through this study has therefore provided an important insight into the specific kinds of support AS patients need, want and crucially, would be willing to recruit into. Such data will be invaluable in informing the development and design of any subsequent AS specific support interventions.

There is growing evidence to support the distress inducing nature of AS (Burnet et al., 2007, van den Bergh et al., 2009; van den Bergh, 2010). This distress currently acts as a significant predictor in determining which AS patients will go on to transfer to clinically unnecessary radical intervention (Latini et al., 2007; Patel et al., 2004). To help prevent this there is an urgent need to develop and provide support interventions that AS patients are firstly willing to recruit into and adhere to and secondly that are effective at making available and sharing information and support to help them better cope, manage and live with the uncertainty of AS. Through doing so it may be possible to lower the high levels of anxiety associated with AS and so lower the number of men transferring to radical treatment.

To date, very few investigations have attempted to specifically ask AS patients what kind of support they require to help them cope with AS. Therefore the findings of the current investigation provide a novel insight into exactly what types and formats of interventional support AS patients want and would be willing to take part in. Now that such information is available, it is crucial that it be used to design, develop and pilot an AS specific support intervention which may provide men being managed with AS with an effective form of support to help them better manage the uncertainty and distress of their condition in a way that is acceptable to them.

Chapter 8

Discussion and Conclusion

8.1 Introduction

From its inception in 2010, the National Cancer Survivorship Initiative (NCSI, 2010) has advocated the need for a substantial increase in research focusing specifically on the assessment and management of psychological conditions such as depression and anxiety in cancer recovery and survival. This call seems to have been heeded; the last several years have seen a substantial increase in research activity relating to the assessment and management of these conditions among most common cancer sites (Rayner et al., 2011; NICE, 2011).

Yet despite being the most common form of male cancer in the UK (Office for National Statistics, 2010), very little of this research attention has been given to the assessment and management of depression and anxiety in men diagnosed with PCa. This would appear to be particularly true for PCa patients diagnosed with localised disease who are being managed with AS. Indeed, the last UK based investigation to specifically assess or address these conditions in a cohort of AS patients was conducted over 6 years ago (Burnet at al., 2007).

Increasingly, more and more men with localised PCa who are suitable for management with AS are being diagnosed (NICE, 2014). Men being managed with AS who are clinically anxious are significantly more likely to transfer to clinically unnecessary radical intervention in the absence of any meaningful signs of disease progression (Patel et al., 2004; Latini et al., 2007). Consequently, the assessment and management of anxiety in this patient group has been highlighted as an area of key address and one that must be attended to as a matter of clinical urgency (Pickles et al., 2007).

The foundation of research into the assessment and management of anxiety and depression among AS patients is still very poor, both in the UK and globally. My primary motivation for undertaking this PhD was to begin to address this issue and provide an initial insight into the prevalence of depression and anxiety specifically in PCa patients being managed with AS. Having established this, it was then my aim to determine how to manage these conditions with a supportive intervention. To that end, the data collected over the course of this PhD has

added new evidence to current knowledge about the prevalence of psychological distress in this patient group and how best we can manage it.

8.2 How this PhD has added to the related research

8.2.1. The Systematic Review and Meta-Analysis

The data searching process conducted as part of the systematic review revealed that a small but clinically meaningful foundation of research evidence currently exists relating to the measurement of depression and anxiety in PCa. Yet this evidence had not been previously subjected to a rigorous systematic review and meta-analysis of prevalence rates. This represented an important limitation in our understanding of the management of survivorship in this population as healthcare professionals working with PCa were unable to access an appropriate and informed evidence synthesis. Reviews and meta-analyses of this nature currently exist for many other cancer sites (Reich et al., 2008; Mitchell et al., 2011). The systematic review and meta-analysis overviewed in Chapter 3 has gone some way to addressing this issue.

Furthermore, by stratifying the results as a function of treatment stage (pre, on and post-treatment) I hoped to increase the clinical applicability of the data by allowing clinicians to more readily determine at what point of the treatment spectrum their patients are most likely to experience psychological distress.

The results of the meta-analysis revealed that across the trajectory of treatment, men with PCa experienced a high prevalence of depression and anxiety that is similar to that observed within other common cancer sites (Kugaya et al., 2000; Wong-Kim & Bloom, 2005). These results question the unfounded assumption that male cancer patients, particularly older ones, are less disposed to psychological distress due to the inherent trait psychological profiles to this patient demographic (Brod, 1995).

Furthermore, the results highlighted an interesting trajectory of distress across the treatment spectrum. It was observed that patients experienced the highest level of psychological distress in the ‘pre-treatment phase’, which then dropped off during the ‘on-treatment phase’ before rising again after the cessation of treatment. These findings are important and clinically relevant and will be of interest to those working with PCa as they highlight the impact that different phases of treatment can have upon psychological wellbeing.

However, when interpreting these findings it is important to be aware of several key limitations that may have impacted upon the generated results. Firstly, the majority of studies entered into this review were cross-sectional in design. It is highly likely that anxiety and depression within PCa are not linear constructs but ones that peak and trough at differing times, such as prior to PSA tests. As a result, the meta-analysis was not able to account for the ways in which depression and anxiety may longitudinally fluctuate across the cancer journey. This is an important issue that needs to be addressed by well designed, prospective longitudinal research studies.

Secondly, a high level of heterogeneity was observed across the included studies. Whilst this was to be expected in light of the observed variation in sample size, sample characteristics and the differing questionnaires used, it still suggests that substantial differences existed in the prevalence of depression and anxiety observed across the studies. This limits the confidence we can have in drawing conclusions from the prevalence data generated and as such caution must be observed when interpreting the clinical relevance of the findings.

Furthermore, this study did not compare the depression and anxiety prevalence rates generated directly to that observed in a cohort to healthy men or men with other cancers. As a consequence, we were unable to specifically determine how PCa and its treatment impacted on the prevalence of psychological distress observed. The essentially descriptive nature of this study therefore needs to be noted.

Lastly, it was not possible to formally assess how the prevalence of depression and anxiety varied as a function of either treatment type or disease stage. This is a key limitation. The physical side effects of each of the differing treatment modalities for PCa vary greatly and one would expect this variation to have differing impacts upon the degree of psychological distress experienced.

Likewise, one would also expect disease stage to have a substantial impact upon the prevalence of psychological distress observed. Men living with localised PCa have an extremely good prognosis and can expect to live for many years. In contrast, those with metastatic disease experience much higher rates of morbidity and a significantly reduced life expectancy. It is likely that this would greatly impact upon the degree of depression and anxiety experienced. The fact that the majority of the participants included within the meta-analysis had localised PCa suggests that the prevalence data generated may be an under-

representation and not applicable to men with advanced or metastatic disease. This important limitation needs to be accounted for when interpreting the findings of this review.

Despite these limitations, the findings of this review clearly contradict the assumption that these men do not experience psychological distress. These data may provide a means of stratifying the screening for psychological distress in PCa patients to ensure that those at the greatest risk of developing depression and anxiety are offered a timely and appropriate level of support.

8.2.2. The Depression and Anxiety Cross-Sectional Prevalence Survey

The evidence into the prevalence of depression and anxiety specifically among AS patients is limited, particularly in the UK. The aim of the cross-sectional Hospital Anxiety and Depression Scale questionnaire postal survey conducted in Chapter 4 was to address this issue and provide a larger, more generalizable and definitive estimate of psychological distress among AS patients in the UK.

Utilising a cross-sectional design was deemed the most appropriate methodology to adopt given my research questions and the time and financial restrictions placed upon this as part of a PhD project. However, utilising a cross-sectional methodology in this way resulted in several important limitations that need to be taken into account when interpreting the findings. The inability of a cross-sectional survey to account for changes in depression and anxiety over time is important and it would be very helpful for future longitudinal cohort based research to address this.

Likewise, due to the anonymous recruitment approach recommend by the Research Ethics Committee, I was unable to screen patient records to assess a relevant past history of depression and anxiety. It may have been that the anxiety and depression observed in any individual patient had little to do with their PCa or management with AS but to an underlying history of, and predisposition to, such conditions. To allow for a greater understanding of the specific anxiety and depression inducing nature of AS, future research into men without any confirmed past history of such conditions is important. However, the prevalence rates observed in this study are much greater than that reported in the general population of men aged over 65 in the UK (Department of Health, 2011) and compare well with that observed among breast cancer patients (Pasquini & Biondi, 2007; Wong-Kim & Bloom, 2005), suggesting that these prevalence rates are most likely to be PCa related.

However, as I failed to recruit a cohort of PCa patients who were receiving radical treatment it is not possible to determine how the prevalence rates of depression and anxiety observed in the AS patients compare to those seen in patients receiving radical treatment. This means that we are still unclear as to how distress inducing AS is in comparison to radical treatment.

Likewise, whilst our findings suggest that AS patients experience a much greater prevalence of anxiety and depression when compared to men of a similar age without PCa (Department of Health, 2011) these conclusions are drawn from indirect comparisons with previously conducted research rather than from direct comparison with an age matched control group.

Lastly, depressed and anxious cancer patients are less likely to complete and return questionnaires than their non-depressed and non-anxious counterparts (Schofield et al., 2003). It is therefore possible that the prevalence data generated represents an underestimate of distress. This limits the generaliseabilty of the findings.

Despite these limitations, this study is currently the largest of its kind to be undertaken to quantify depression and anxiety prevalence specifically in a sample of AS patients and has revealed a high prevalence of both. In light of the increasing use of AS in the UK (NICE, 2014), these data are important as they provide those involved in the management of AS patients with a large, geographically varied, appropriately powered and more definitive estimate of the prevalence of psychological distress in the patients they treat. With additional supporting evidence, these results suggests that it may be beneficial for men who are placed onto an AS protocol to be routinely followed up with psychological screening processes (i.e. the administration of brief, valid and reliable questionnaires) to identify men who may be developing depression and anxiety which in turn will affect their quality of life and survivorship. Such men could then be properly supported in a more efficient and timely fashion. Given the clear clinical and economic benefits of keeping men who are suitable for AS on this management pathway, it is hoped that these data will impact on the assessment of psychological distress in this population and thus have a positive impact upon the way in which AS patients in the UK are managed and supported.

8.2.3. The Mindfulness Based Stress Reduction Study

In recent years the utilisation of mindfulness based support interventions as a tool to manage psychological distress among cancer patients has exploded (Carlson et al., 2003; Carlson et al., 2007; Garland et al., 2007; Wite-Janusek et al., 2008; Lengacher et al., 2010; Speca et al., 2000). Yet MBSR has never been trialled exclusively within a male specific cancer population.

This represented a substantial limitation into our understanding of how it may be possible to better manage psychological distress in male cancer patients with mindfulness based approaches.

The MBSR investigation overviewed in Chapter 6 was, to the best of my knowledge, the first of its kind to trial the use of a standardised MBSR intervention exclusively within a sample of AS patients. My methodological rationale for doing so included a comprehensive literature review of the use of self-care interventions in PCa, the results of which highlighted that PCa patients appeared willing to recruit into group based support interventions and found benefit in doing so (Chapter 5). Likewise, my decision to utilise an MBSR intervention was based on a theoretical rationale; the majority of stressors faced by AS patients have been shown to be caused by fears of what "may" happen in the future, not by what is actually happening at the present time (Hedestig, Sandman & Widmark, 2003; Kronenwetter et al., 2005). MBSR grounds individuals in the present moment and so lowers ruminative anxiety (Kabat-Zinn, 1990). I posited that empowering AS patients with mindfulness techniques would allow them to live more mindfully in the present moment which may help to lessen the psychological distress they experience as a result of ruminative anxiety about the future.

Despite this methodological and theoretical rationale, I was unable to recruit a sample of AS patients into the proposed MBSR intervention. This revealed valuable findings and insights into important barriers and issues that may prevent AS patients from recruiting into self-care interventions, data that was largely missing from the previously conducted research.

However, it is also important to be aware of the possible methodological limitations that may account for my inability to successfully recruit into this trial. Firstly was the assumption that AS patients would find MBSR an acceptable form of support and one that they would be willing to recruit into. Whilst I feel that the literature review conducted in Chapter 5 supported the view that PCa patients are willing to recruit into time demanding group interventions, this evidence was not specific to MBSR, was not conducted with AS patients and were not UK based. Looking back reflectively I can see that I to a degree failed to objectively assess whether enough of a rationale existed for trialling an MBSR intervention in this way, which ultimately played a part in the failure of the investigation.

To have addressed this issue it would have been good practice to have conducted an initial qualitative scoping study to assess the kinds of support AS patients require and would be willing to recruit into. Ideally this would have involved interviewing a small sample of AS patients to better determine their views on AS, whether they found it acceptable and whether

they would recruit into it. This information would have been hugely beneficial in the initial design and planning stage of the MBST trial. However, it is important to be aware of the fact that conducting a scoping exercise in this way would have required time and financial resources in excess of that which were available to me as a 3-year PhD project which would have made such an exercise largely impractical and whilst this study ultimately failed, it did server to stimulate me to consider how I might redesign the intervention for this specific patient group.

8.2.4. The Qualitative Interview Study

To address this issue and allow me to design an AS specific support intervention that would be deemed acceptable for AS patients to recruit into, I subsequently decided to recruit and qualitatively interview 20 AS patients. Adopting a methodological approach of this nature allowed me to determine the kinds of issues and problems that are routinely experienced by men being managed with AS and how it may be possible to design a support intervention that would effectively address these issues in a format and structure that patients would find acceptable and recruit into.

A small foundation of qualitative research into the experiences of AS patients currently exists but the majority of this has focused on the decision making process that men adopt when choosing to select AS (Davidson & Goldenberg, 2011; Davidson et al., 2009). To date no UK based investigation has qualitatively interviewed a cohort of AS patients to determine what kinds of support they would like to allow them to better manage the unique problems and stressors associated with being managed with AS and in what format such support should be packaged to help maximise patient recruitment and adherence.

The qualitative interviews conducted as part of this study generated three themes:

1) Route to diagnosis

2) Problems of living with PCa and being managed with AS.

3) Managing life and survivorship under AS.

8.3. The Way Forward

The findings from the qualitative study may provide an interesting and unique means of designing, developing and piloting an AS specific psycho-educational support intervention to

help empower those being managed with AS with an effective means of managing the psychological distress often associated with this management approach.

More specifically, a key theme to emerge from the qualitative data highlighted that AS patients reported levels of anxiety, concern and distress as a result of their management with AS (Theme 1: problems of living with PCa and being managed with AS). This was predominantly due to the uncertainty commonly experienced with this management approach and a poor understanding of what AS was, what it entailed and why it was a safe and clinical suitable management approach for them.

Having identified these problems and concerns in Theme 1, Theme 2 (managing life and survivorship under AS) provided a novel insight into the ways in which the interviewees believed that their problems and concerns could be better managed to help lower the levels of distress they were experiencing. Two predominant ways of doing so emerged: 1) group based support and 2) by having access to a psycho-educational AS specific support website.

Based on this evidence it would appear that if we are to successfully design and develop a support intervention for AS patients in a structure and format that will be acceptable for them the recruit into, it must aim to utilise both of these two specific forms of support. I plan to do so in the following ways:

8.3.1. Group Support

The use of group based interventions as a means of supporting cancer patients through the psychological dysfunction caused by diagnosis and treatment is well established (Fors et al., 2011; Antonio et al., 2006). The findings from the qualitative interview study (chapter 7) have revealed that AS patients were positive about the use of group support as long as it was offered in a structure and format that was deemed acceptable to them; they wanted only 2-4 group sessions and believed that each session should last for no more than 60-90 minutes. This was in stark contrast to the 8 two-hour sessions that make up a standardised MBSR programme.

Likewise, they wanted the groups to be relatively small (10 AS patients or less) and to be facilitated by a suitably qualified PCa nurse. This last point was of particular importance to the interviewees as they felt it would provide them with access to safe and accurate clinical information and answers to any questions or queries they may have.

Relating to the content of the group sessions, the key benefit that the interviewees believed they would obtain from group support was access to more detailed information about AS that was not currently being provided to them in an effective way during their clinic appointments. For example, what AS is and what it entails, why it is clinically suitable and safe, why radical treatment was not advised and when (if ever) initiation of radical treatment becomes necessary and why. These were common concerns articulated by the interviewees and ones that they believed would be best addressed though a PCa nurse led group support intervention. Furthermore, the interviewees also articulated a degree of emotional distress and stated that they would like help and guidance on self-care interventions that would allow them to better manage such distress.

8.3.2. Internet Support

During the qualitative study, the interviewees were also extremely positive of and interested in the concept of an AS specific informational website. The primary reason for this was the belief that so much anecdotal, misleading and contradictory evidence about PCa, AS and lifestyle interventions (diet, exercise and stress management) currently exists on the internet that the interviewees did not know where to look for safe and trustworthy information. They believed that an informational website designed specifically for AS patients would remedy this situation. There was also the belief that a website would offer a good accompaniment to the group sessions by providing attendees with supporting information to that received in the group sessions that they could access at their own leisure and read in the privacy and convenience of their own home.

8.4. The PRO-ACTIVE Intervention

These findings have now been used to design an AS specific support intervention entitled **PRO-ACTIVE**: **PRO**state Cancer Support Intervention for **ACTIVE** Surveillance Patients.

PRO-ACTIVE is a 6-week group and internet based intervention. The group support component will consist of three 90-minute group support sessions delivered once a fortnight for 6-weeks. Each group will be made up of 8-10 AS patients and will be facilitated by a PCa nurse specialist and a Macmillan Support nurse. Each of the three sessions will address a specific area:

Session 1: Active Surveillance Information Session

The first session will introduce patients to the intervention. Ground rules for the group sessions will be established by the facilitators. The facilitators will place AS in context by

comparing the likelihood of dying from PCa versus dying from other causes, in men with a localised PCa diagnosis. Information on PCa and treatment related morbidity, such as erectile dysfunction and incontinence, will also be addressed. Group discussions about PCa and AS will then be initiated by the facilitators to allow key issues and questions about this management approach to be addressed.

Session 2: Introduction to Stress Management and Relaxation and Resilience Techniques Training

The second session will introduce participants to two simple to learn and easy to practice breath based relaxation and resilience techniques; a whole body relaxation technique and a technique they can use in moments of stress. This session will also provide an opportunity to discuss lifestyle issues (exercise, stress and diet) and AS specific information.

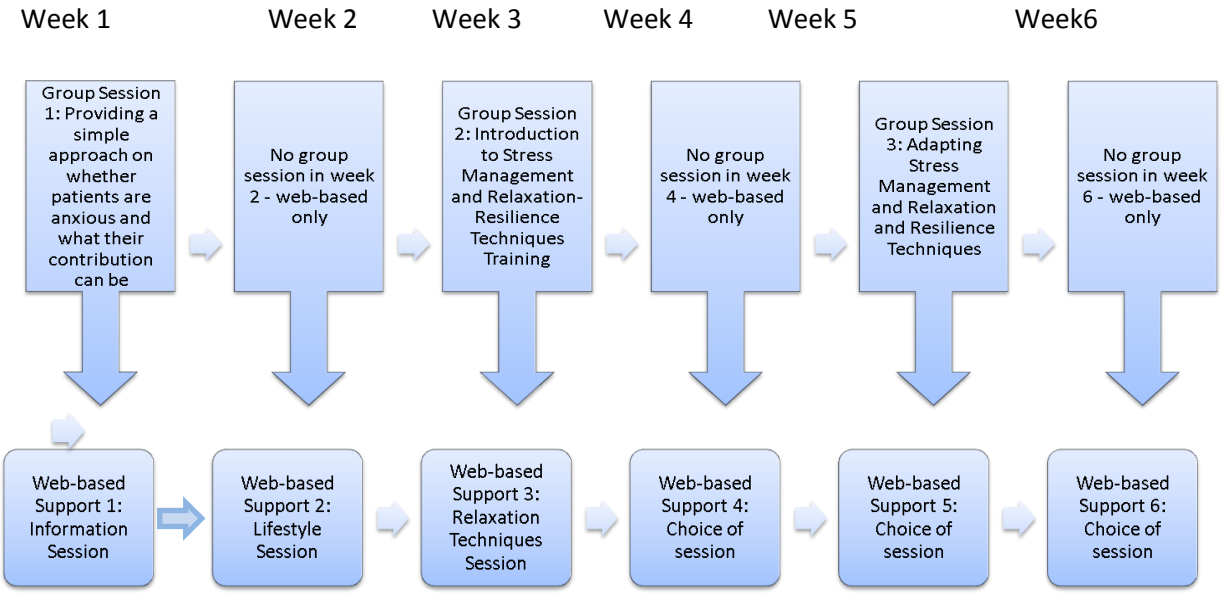
Session 3: Adapting Stress Management and Relaxation and Resilience Techniques

The third session will allow participants to provide feedback on the intervention, receive answers to any possible queries they may have as a result of the previous group sessions and discuss the effects of the relaxation techniques and any problems they may have encountered whilst practising them at home. There will also be the opportunity to discuss issues around the internet-support programme (access to the website, the content of the website, feedback from the group for improvement) and their role in the group (possible future groups as expert patients, the dynamics within the group).

Internet Intervention

The internet intervention will consist of 6 online modules that will be released once a week for the 6-week intervention duration. The online modules will support the group sessions and will cover areas such as PCa and AS information, diet and nutrition, exercise, goal setting, stress management and relaxation , frequently asked questions and a links page to relevant support charities. Figure 12 below provides a schematic of the timeline of PRO-ACTIVE:

Figure 12: PRO-ACTIVE content timeline



8.5. Conclusion

Much debate currently exists into whether or not the utilisation of AS for the management of localised PCa predisposes patients to psychological morbidity. My overriding motivation for undertaking this PhD was to further investigate this issue and better define both the prevalence of depression and anxiety in this patient group and how best to manage it.

The systematic review and meta-analysis conducted in Chapter 3 highlighted a relatively high prevalence of depression and anxiety in generic PCa patients that varied as a function of treatment stage. The review also highlighted a paucity of data relating to the assessment of depression and anxiety specifically in men being managed with AS. To address this issue I sought to better define the specific prevalence of depression and anxiety in a large sample of AS patient recruited from multiple centres across the UK utilising the Hospital Anxiety and Depression Scale. The results highlighted a high prevalence of both depression and anxiety. These findings provided a strong rationale for the need for interventional support that would allow AS patients to better manage their distress.

My initial aim was to do so through the use of a standardised 8-week Mindfulness Based Stress Reduction programme. Unfortunately this form of support was deemed unacceptable to the AS patient I approached for recruitment. To address this issue it was fundamental to ascertain exactly what kinds of support AS patients would like to help them better cope and manage with their distress and uncertainty. A qualitative approach was deemed the best means of

doing so. The qualitative study described in Chapter 7 is the first of its kind to specifically ascertain exactly what kinds of supportive assistance AS patients in the UK would like and would be willing to recruit into.

The themes that emerged from this qualitative study have now been used to develop the PRO-ACTIVE intervention. The development of this intervention has been a collaborative effort from a team of urological surgeons, academics, health psychologists, urological nurse specialists, Macmillan nurses and clinicians from the University of Southampton, Southampton University Hospitals NHS Trust and University College London Hospitals NHS Trust Foundation.

The first preliminary evaluation of the PRO-ACTIVE intervention among a group of 10 AS patients from University College London Hospitals is currently underway. If the results from this initial pilot suggests effectiveness, I aim to generate additional funding to allow me to further assess the application and effectiveness of PRO-ACTIVE in a larger multi-centre study (at Southampton University Hospitals NHS Trust and University College London Hospitals NHS Trust Foundation).

It is my hope that in time, PRO-ACTIVE will offer a clinically effective and economically sustainable form of support that can be offered as a part of routine care to all men in the UK who are placed onto an AS management pathway within the NHS. Doing so may help to improve the psychological health and wellbeing of this patient group and in doing so help lower the number of men who are transferring to clinically unnecessary radical intervention in the absence of any meaningful levels of disease progression. This in turn will have a substantial impact upon improving the quality of life and survivorship of this patient group.

Appendices

Appendices

Appendix 1

List of questionnaires identified to measure psychological health in the prostate cancer literature.

1. Hospital Anxiety and Depression Scale (HADS)
2. Profile of Mood States (POMS)
3. Memorial Anxiety Scale for Prostate Cancer (MAX-PC)
4. SF-36 Health Survey
5. Cancer Rehabilitation Evaluation System-Short Form (CARES-SF)
6. Brief Symptom Inventory (BSI)
7. UCLA Prostate Cancer Index (UCLA-PCI)
8. Stait -Trait Anxiety Scale (STAI)
9. General Health Questionnaire – 30 (GHQ-30)
10. European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire C30 (EORTC-QLQ-C30)
11. The Mental Adjustment to Cancer Scale (MAC-Scale).
12. Expanded Prostate Cancer Index Composite (EPIC)
13. Positive Affect Negative Affect Scale (PANAS)
14. Composite International Diagnostic Interview (CIDI)
15. Centre for Epidemiologic Studies Depression Scale (CES-D)
16. Impact of Event Scale (IES)
17. Symptom Checklist-90 (SCL-90)
18. Functional assessment of Cancer Therapy – Prostate (FACT-P)
19. SF-12 Health Survey
20. Medical Outcome Study – Short Form (MOS-SF)
21. Quality of Life Scale – Patient Version (QOL-PV)
22. Functional Living Index: Cancer (FLI-C)
23. Support Care Needs Survey (SCNS)
24. Prostate Cancer Specific Quality of Life Instrument (PROSQOL1)
25. RAND-36 Health Survey
26. Mini Mental Adjustment to Cancer Scale (mini-MAC)
27. Prostate Cancer Quality of Life Scale (PC-QOL)
28. Beck Depression Inventory (BDI)
29. The Distress Thermometer
30. Generalised Anxiety Disorder Questionnaire (GAD-Q)
31. Multidimensional Fatigue Inventory
32. Self Rating Anxiety Scale (SAS)
33. Self Rating Depression Scale (SDS)
34. Effects of Prostate Cancer on Lifestyle Questionnaire (EPCLQ)
35. Decision Related Distress
36. European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire – PR25
37. Revised Illness Perception Questionnaire (IPQ-R)
38. Abridged Stait-Trait Anxiety Scale – 6 (STAI-6)
39. Quality of Life Index (QLI)
40. Geriatric Depression Scale

Appendix 2

Pre-Treatment Depression Prevalence Meta-Analysis

Study ID	ni	%	ri	pi	logit pi	SEi	wi	Li	Ui	wilogitpi	Qi		%	Lower %	Upper %
3	123	11	14	0.114	-2.052	0.284	12.407	-2.609	-1.496	-25.462	2.924		11.38	6.86	18.30
5	50	10.4	5	0.100	-2.197	0.471	4.500	-3.121	-1.273	-9.888	1.788		10.00	4.22	21.87
9	83	5	4	0.048	-2.983	0.513	3.807	-3.988	-1.979	-11.358	7.637		4.82	1.82	12.15
20	115	13.5	16	0.139	-1.823	0.269	13.774	-2.351	-1.294	-25.103	0.901		13.91	8.70	21.51
21	84	15.5	13	0.155	-1.698	0.302	10.988	-2.289	-1.106	-18.655	0.188		15.48	9.20	24.85
34	36	22	8	0.222	-1.253	0.401	6.222	-2.039	-0.467	-7.795	0.614		22.22	11.52	38.53
35	40	25	10	0.250	-1.099	0.365	7.500	-1.814	-0.383	-8.240	1.644		25.00	14.01	40.54
47	103	28.2	29	0.282	-0.937	0.219	20.835	-1.366	-0.507	-19.518	8.271		28.16	20.32	37.58
49	50	2	1	0.020	-3.892	1.010	0.980	-5.872	-1.912	-3.814	5.297		2.00	0.28	12.88
53	118	10.2	12	0.102	-2.179	0.305	10.780	-2.776	-1.582	-23.484	4.034		10.17	5.87	17.06
57	40	25	10	0.250	-1.099	0.365	7.500	-1.814	-0.383	-8.240	1.644		25.00	14.01	40.54
59	229	22	50	0.218	-1.275	0.160	39.083	-1.589	-0.962	-49.845	3.320		21.83	16.95	27.65
63	118	12	14	0.119	-2.005	0.285	12.339	-2.563	-1.447	-24.744	2.373		11.86	7.15	19.04
			fr				150.715			-236.143	40.635	Cochran's Q			

meta analysis	logit(p) =	-1.567	p =	0.173	**meta analysis**	**17.27**	**15.06**	**19.72**
	lower limit	-1.730	lower limit p	0.151				

Appendix 3. On-Treatment Depression Prevalence Meta-Analysis

Study ID	ni	%	ri	pi	logit pi	SEi	wi	Li	Ui	wilogitpi	Qi	%	Lower %	Upper %
5	50	16.7	8	0.16	-1.658	0.386	6.720	-2.414	-0.902	-11.143	0.067	16.00	8.21	28.86
14	51	51	26	0.51	0.039	0.280	12.745	-0.510	0.588	0.500	41.181	50.98	37.52	64.30
34	36	19	7	0.19	-1.421	0.421	5.639	-2.247	-0.596	-8.015	0.640	19.44	9.56	35.53
35	40	18	7	0.18	-1.551	0.416	5.775	-2.366	-0.735	-8.955	0.249	17.50	8.58	32.41
38	45	13.3	6	0.13	-1.872	0.439	5.200	-2.731	-1.012	-9.733	0.067	13.33	6.12	26.65
46	62	3	2	0.03	-3.401	0.719	1.935	-4.810	-1.992	-6.583	5.224	3.23	0.81	12.00
54	129	8	10	0.08	-2.477	0.329	9.225	-3.122	-1.831	-22.846	4.758	7.75	4.22	13.81
55	129	8	10	0.08	-2.477	0.329	9.225	-3.122	-1.831	-22.846	4.758	7.75	4.22	13.81
1	181	4	13	0.07	-2.559	0.288	12.066	-3.123	-1.995	-30.878	7.736	7.18	4.22	11.98
							68.530			-120.498	64.682			
Meta-Analysis					logit(p) =	-1.758		p =	0.147		**Meta-Analysis**	**14.70**	**11.92**	**17.99**
					lower limit	-2.000		lower limit p	0.119					
					upper limit	-1.51673		upper limit p	0.180					

Appendix 4: Post-Treatment Depression Prevalence Meta-Analysis

Study ID	ni	%	ri	pi	logit pi	SEi	wi	Li	Ui	wilogitpi	Qi	%	Lower %	Upper %
3	123	9	11	0.09	-2.314	0.315	10.074	-2.931	-1.696	-23.307	6.890	9.00	5.06	15.50
7	195	16	31	0.16	-1.658	0.195	26.208	-2.041	-1.275	-43.459	0.772	16.00	11.50	21.83
21	84	52	44	0.52	0.080	0.218	20.966	-0.348	0.508	1.678	51.460	52.00	41.39	62.44
22	861	17	146	0.17	-1.586	0.091	121.487	-1.763	-1.408	-192.633	1.191	17.00	14.64	19.66
35	40	30	12	0.3	-0.847	0.345	8.400	-1.524	-0.171	-7.117	3.433	30.00	17.89	45.73
41	327	2.4	8	0.024	-3.705	0.361	7.660	-4.414	-2.997	-28.382	37.709	2.40	1.20	4.76
48	326	8.6	28	0.086	-2.363	0.198	25.625	-2.751	-1.976	-60.564	19.703	8.60	6.00	12.17
50	183	12.6	23	0.126	-1.937	0.223	20.153	-2.373	-1.500	-39.032	4.084	12.60	8.52	18.24
51	150	26.6	40	0.266	-1.015	0.185	29.287	-1.377	-0.653	-29.726	6.513	26.60	20.15	34.24
57	40	30	12	0.3	-0.847	0.345	8.400	-1.524	-0.171	-7.117	3.433	30.00	17.89	45.73
59	229	15.5	35	0.155	-1.696	0.183	29.993	-2.054	-1.338	-50.866	1.314	15.50	11.37	20.78
62	381	26	99	0.26	-1.046	0.117	73.304	-1.275	-0.817	-76.674	14.233	26.00	21.84	30.64
1	148	9	13	0.09	-2.314	0.287	12.121	-2.877	-1.751	-28.044	64.884	9.00	5.33	14.80
							393.678			-585.244	215.620			

Meta-Analysis	logit(p) =	-1.48661	p =	0.184432	**Meta-Analysis**	**18.44**	**15.18**	**22.22**
	lower limit	-1.7202	lower limit p	0.151845				
	upper limit	-1.25301	upper limit p	0.22218				

Appendix 5: Pre-Treatment Anxiety Prevalence Meta-Analysis

Study ID	ni	%	ri	pi	logit pi	SEi	wi	Li	Ui	wilogitpi	Qi		%	Lower %	Upper %
3	123	23.0	28	0.228	-1.222	0.215	21.626	-1.643	-0.800	-26.420	1.135		22.76	16.20	31.00
9	83	31.2	26	0.313	-0.785	0.237	17.855	-1.249	-0.321	-14.016	0.769		31.33	22.29	42.04
18	67	22.0	15	0.224	-1.243	0.293	11.642	-1.818	-0.669	-14.473	0.731		22.39	13.97	33.88
20	115	25.2	29	0.252	-1.087	0.215	21.687	-1.508	-0.666	-23.575	0.194		25.22	18.12	33.94
21	84	25.0	21	0.250	-1.099	0.252	15.750	-1.592	-0.605	-17.303	0.177		25.00	16.90	35.33
49	50	30.0	15	0.300	-0.847	0.309	10.500	-1.452	-0.242	-8.897	0.221		30.00	18.97	43.97
53	118	15.3	18	0.153	-1.715	0.256	15.254	-2.217	-1.213	-26.158	7.958		15.25	9.83	22.92
59	229	28.0	64	0.279	-0.947	0.147	46.114	-1.236	-0.658	-43.672	0.095		27.95	22.52	34.11
63	118	12.0	46	0.390	-0.448	0.189	28.068	-0.818	-0.078	-12.575	8.322		38.98	30.62	48.05
							188.496			-187.089	19.604	Cochran's Q			

logit(p) =	-0.993	p =	0.270	**meta analysis**	**27.04**	**24.26**	**30.01**
lower limit	-1.138	lower limit p	0.243				
upper limit	-0.847	upper limit p	0.300				

Appendix 6

On-Treatment Anxiety Prevalence Meta-Analysis

Study ID	ni	%	ri	pi	logit pi	SEi	wi	Li	Ui	wilogitpi	Qi		%	Lower %	Upper %
46	62	15	9	0.15	-1.773	0.361	7.694	-2.480	-1.066	-13.641	0.016		14.52	7.73	25.61
54	129	17	22	0.17	-1.582	0.234	18.248	-2.041	-1.123	-28.865	0.387		17.05	11.50	24.55
55	129	12	15	0.12	-2.028	0.275	13.256	-2.566	-1.490	-26.885	1.199		11.63	7.13	18.39
1	181	16	28.96	0.16	-1.658	0.203	24.326	-2.056	-1.261	-40.339	0.116		16.00	11.35	22.08
							63.524			-109.729	1.718	Cochran's Q			
Meta-Analysis					logit(p) =	-1.727		p =	0.151		**Meta-Analysis**		**15.09**	**12.15**	**18.60**
					lower limit	-1.978		lower limit p	0.121						
					upper limit	-1.47644		upper limit p	0.186						

Appendix 7

Post-Treatment Anxiety Prevalence Meta-Analysis

Study ID	ni	%	ri	pi	logit pi	SEi	wi	Li	Ui	wilogitpi	Qi		Lower %	Upper %
3	123	8	10	0.08	-2.442	0.332	9.053	-3.094	-1.791	-22.110	8.326	8.00	4.34	14.30
7	195	11.8	23	0.118	-2.012	0.222	20.295	-2.447	-1.576	-40.823	5.661	11.80	7.97	17.13
21	84	15.5	13	0.155	-1.696	0.301	11.002	-2.287	-1.105	-18.658	0.497	15.50	9.22	24.88
22	861	23.7	204	0.237	-1.169	0.080	155.695	-1.326	-1.012	-182.039	15.365	23.70	20.98	26.66
41	327	10.7	35	0.107	-2.122	0.179	31.245	-2.472	-1.771	-66.295	12.735	10.70	7.78	14.54
48	326	9.6	31	0.096	-2.242	0.188	28.292	-2.611	-1.874	-63.443	16.304	9.60	6.84	13.31
50	183	12.6	23	0.126	-1.937	0.223	20.153	-2.373	-1.500	-39.032	4.144	12.60	8.52	18.24
51	150	23.3	35	0.233	-1.191	0.193	26.807	-1.570	-0.813	-31.939	2.284	23.30	17.22	30.73
59	229	17.5	40	0.175	-1.551	0.174	33.062	-1.891	-1.210	-51.266	0.150	17.50	13.11	22.97
62	381	23.9	91	0.239	-1.158	0.120	69.296	-1.394	-0.923	-80.256	7.327	23.90	19.88	28.44
1	148	15	22	0.15	-1.735	0.230	18.870	-2.186	-1.283	-32.732	1.191	15.00	10.10	21.70
											73.984	Cochran's Q		
Meta-Analysis					logit(p) =	-1.48334		p =	0.18492		**Meta-Analysis**	**18.49**	**13.81**	**24.31**
					lower limit	-1.83117		lower limit p	0.13809					
					upper limit	-1.13551		upper limit p	0.24314					

Appendix 8

Berkshire Research Ethics Committee Approval Letter.

NHS

National Research Ethics Service
NRES Committee South Central - Berkshire

Building L27
University of Reading
London Road
Reading
RG1 5AQ

Telephone: 0118 918 0551
Facsimile: 0118 918 0559

11 May 2011

Prof George Lewith
Professor of Health Research
University of SOuthampton
Primary Medical Care
Aldermoor Health Centre
Aldermoor Close, Southampton
SO16 5ST

Dear Prof Lewith

Study title: **The incidence of clinical levels of depression and anxiety within prostate cancer patients under active surveillance**

REC reference: **11/SC/0071**
Protocol number: **1**

Thank you for your letter of 6 April 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Protocol	2	10 May 2011
Letter of invitation to participant	2	06 April 2011
Response to Request for Further Information	2	06 April 2011
REC application	3.1	18 February 2011
Participant Consent Form	1	18 February 2011
Questionnaire: Hospital Anxiety and Depression Scale (HADS)	2	06 April 2011
Questionnaire: Patient Demographic	2	06 April 2011
Letter from National Institute for Health Research, School for Primary Care Research		22 April 2010
Summary of Investigation Protocol	1	18 February 2011
Letter from Funder		22 April 2010
Participant Information Sheet	1	18 February 2011
Referees or other scientific critique report	1	18 February 2011
Referees or other scientific critique report		06 April 2011
Investigator CV	Prof George Lewith, v2	06 April 2011
Investigator CV	Sam Watts, v2	06 April 2011
Investigator CV	Dr Geraldine Marie-Clare, v2	06 April 2011
Covering Letter		18 February 2011
Letter from Sponsor		14 February 2011

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

This Research Ethics Committee is an advisory committee to South Central Strategic Health Authority

The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England

Appendix 9

Cross-Sectional Anxiety and Depression Survey Patient Information Pack Contents

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PATIENT INVITATION LETTER

[Southampton University Headed Paper]

TO A UNIVERSITY OF SOUTHAMPTON RESEARCH PROJECT

Project Title: The incidence of clinical levels of depression and anxiety within prostate cancer patients under active surveillance

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear to you or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

Study Overview

This study is being undertaken to allow us to better understand what percentage of men with prostate cancer undergoing active surveillance experience depression and anxiety. To date, very little research has addressed this issue which means that we do not adequately understand the psychological requirements of active surveillance patients. It is thus essential to accurately determine the likely incidence of depression and anxiety in this population which in turn will allow us to better understand, and provide support for, the psychological requirement of these patients.

To do so, we plan to recruit 300 active surveillance patients from the prostate cancer clinic at Southampton University Hospitals Trust. All participants will be asked to anonymously complete the Hospital Anxiety and Depression Scale (HADS) which is a widely used, valid and reliable questionnaire. This will provide us with an initial baseline assessment of the prevalence of clinically significant depression and anxiety within this specific population.

We will also ask participants to anonymously complete a brief questionnaire to measure participant demographics (i.e. age, ethnicity and education, employment and relationship status). This will allow us to determine if any of these factors positively or negatively impact upon the level of depression and anxiety experienced.

Why have I been chosen for this study?

This study is being offered to patients attending Southampton General Hospital who have been diagnosed with prostate cancer and have been deemed eligible to undertake active surveillance by their doctor.

Your participation would involve:

Anonymously completing at home two questionnaires:

1. The Hospital Anxiety and Depression Scale
2. The Participant Demographics Questionnaire.

Both of these questionnaires are to be completed anonymously so it is **important that you do not write your name on either of them.** This will ensure that there will be no breach in confidentiality personal information.

It is important for you to know:

1. It is entirely up to you if you wish to take part in this investigation.
2. Whether or not you take part, your routine care, both now and in the future, will not be affected.
3. The study will involve you taking part in the above.
4. By completing and returning the questionnaires you are consenting to the data collected from the questionnaires to be used anonymously within this investigation.

What to do next if you want to partake in this investigation:

Should you wish to partake in this investigation then please complete the two enclosed questionnaires and post them back to us in the enclosed stamped addressed envelope.

Who to contact if you have questions about your rights as a research participant.

If you require any independent information or advice about your rights as a research subject, or about being involve within this study, you may contact Dr. Martina Prude, head of research governance at the University of Southampton at any time: m.a.prude@soton.ac.uk; 023 8028 848

Who to contact if you have additional questions about this study

If you have any questions regarding this study, your rights as a participant in this research and/or concerns about the study, or if you feel under any pressure to enrol or continue to participate in this study, you may contact the study team at any time: Mr Sam Watts (sw1u09@soton.ac.uk; 07766 480 993), Professor George Lewith (gl3@soton.ac.uk; 023 8024 1073) and Dr Geraldine Leydon (gerry@soton.ac.uk; 023 8024 1048).).

Sources of help and support for depressed and anxious participants

If you are currently feeling depressed or anxious, there are many sources of help available to you. Please find below a list of support networks that you can utilise to help you with the emotions you are feeling.

1. Prostate Cancer Support Organisation (PCaSO) covering Dorset, Hampshire, Sussex and surrounding areas.
   Helpline: 0845 650 2555
   Website: www.pcaso.or

2. Prostate Cancer Charity.
   Helpline: 0800 074 8383
   Website: www.prostate-cancer.org.uk

3. Macmillan Cancer Support
   Helpline: 0808 808 0000
   Website: www.macmillan.org.uk

Who has reviewed this study?

This study was given a favourable ethical opinion for conduct by the Berkshire Research Ethics Committee.

Many thanks for taking the time to read this invitation letter.

Yours sincerely,

Dr. Brian Birch (lead consultant urologist)

Project Title: The incidence of clinical levels of depression and anxiety within prostate cancer patients under active surveillance

Patient Demographics Questionnaire

Instructions for participants: Part of the above titled project involves collecting information about the demographics of prostate cancer patients undergoing active surveillance. Please complete each of the questions below by ticking the box relevant to you. **PLEASE DO NOT WRITE YOUR NAME ON THIS QUESTIONNAIRE.**

Age_____ ☐

Employment: Full Time Employment ☐

Part time Employment ☐

Retired ☐

Unemployed ☐

Relationship Status: Married/Civil Partnership ☐

Co-habiting ☐

Divorced ☐

Widowed ☐

Single ☐

Ethnicity

White British ☐

White Other ☐

Black African ☐

Black Caribbean ☐

Asian ☐

Other (please specify)_____

Education:

Left school before 15 ☐

Completed secondary education ☐

College/specialised training ☐

University ☐

Appendix 10

REC Confirmation Letter

NHS
National Research Ethics Service
NRES Committee South Central - Oxford A
South West Research Ethics Committee Centre
Whitefriars
Level 3 Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 01173421331
Facsimile: 01173420445

19 September 2011

Prof George Lewith
Professor of Health Research
University of Southampton
Primary Medical Care
Aldermoor Health Centre
Aldermoor Close
SO16 5ST

Dear Prof Lewith

Study title:	**Understanding depression and anxiety in prostate cancer: A feasibility study and qualitative evaluation of Mindfulness Based Stress Reduction (MBSR) for the management of depression and anxiety in men with prostate cancer undergoing active surveillance.**
REC reference:	**11/SC/0355**
Protocol number:	**1**

Thank you for your letter of 19 September 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Appendix 11

MBSR Study Insurance and Sponsorship Agreement

UNIVERSITY OF Southampton

Mr Sam Watts
School of Medicine
Primary Medical Care
Aldermoor Health Centre
Aldermoor Close
Southampton
SO16 5ST

RGO REF - 8214

10 August 2011

Dear Mr Watts

Professional Indemnity and Clinical Trials Insurance

Project Title **Understanding Depression and Anxiety in Prostate Cancer: A Feasibility Study and Evaluation of Mindfulness Based Stress Reduction (MBSR) for the Management of Depression and Anxiety in Prostate Cancer Patients undergoing Active Surveliance**

Participant Type:	No Of Participants:	Participant Age Group:	Notes:
Patients	30	Adults	

Thank you for forwarding the completed questionnaire and attached papers.

Having taken note of the information provided, I can confirm that this project will be covered under the terms and conditions of the above policy, subject to written informed consent being obtained from the participating volunteers.

Insurance will only be activated when we have received a copy of the Ethics Committee approval and you must not begin your project prior to this. Please forward a copy of the Ethics Committee approval letter as soon as it is to hand to complete the insurance placement.

If there are any changes to the above details, please advise us as failure to do so may invalidate the insurance.

Yours sincerely

Ruth McFadyen

Mrs Ruth McFadyen
Insurance Services Manager

Tel: 023 8059 2417
email: hrm@soton.ac.uk

cc File

Appendix 12

MBSR Study Patient Invitation Pack Contents

Southampton University Headed Paper]

PATIENT INFORMATION SHEET

1. Title of the Research

Understanding Depression and Anxiety in Prostate Cancer: A feasibility study and evaluation of Mindfulness Based Stress Reduction (MBSR) for the management of depression and anxiety in prostate cancer patients undergoing active surveillance.

Chapter 2: 2. An invitation to join this study

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear to you or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

Chapter 3: 3. What is this study about?

The Mindfulness Based Stress Reduction programme (MBSR) is an eight-week training programme in 'mindfulness'. Mindfulness is a form of Westernised meditation practice which aims to increase your awareness and attention in the present moment, which may help alleviate anxiety, depression and stress (e.g. because you think / worry less about what is happening in the past and in the future and focus instead on the present moment in time).

The aim of the MBSR programme is to teach you how to take time for yourself and live a happier life.

MBSR programmes have been shown to be effective at managing a range of psychological conditions, such as depression, anxiety, fatigue and stress, in a variety of cancer populations. However, it has never been used or assessed exclusively with prostate cancer patients and it is our aim to address this issue and to determine its effectiveness in prostate cancer patients who are undergoing active surveillance.

4. Why have I been chosen for this study?

This study is being offered to you as you are attending Southampton General Hospital and have been diagnosed with prostate cancer and are undergoing active surveillance. In total, there will be approximately 30 patients participating in the study.

Chapter 4: 5. Do I have to take part?

It is completely up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and you will be asked to sign a consent form after you have had a least one day to think about it. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive.

If you decide to take part, we will inform your GP and your oncologist.

6. What will happen to me if I take part?

This study is about exploring your experience of learning the Mindfulness-Based Stress Reduction programme. You will be with other participants who may be in a similar situation to you.

<u>If you take part in the study, you will take part in the following:</u>

A. INITIAL TELEPHONE DISCUSSION WITH MINDFULNESS INSTRUCTOR:

i. One telephone discussion with the mindfulness meditation instructor to tell you about the mindfulness programme.

If you are happy to consent to take part you will then sign a consent form to show you are happy to participate in the mindfulness programme run by the fully trained mindfulness instructor Mr Philip Russell (**B below**).

B. MINDFULNESS MEDITATION PROGRAMME:

i. Eight 2-hour meditation group sessions on a weekly basis over 8 weeks. The first and last class will be 45 minutes longer to allow the collection of blood samples from each participant. During the MBSR sessions the formal practices of 1) mindful body scan (taking the focus of attention through the body), 2) mindful sitting meditation (involving awareness of breathing) and 3) mindful simple gentle slow stretches and mindful walking will be learned.
ii. One 4-5 hour meditation group session will replace the 2-hour session in week 6
iii. Daily home practice of meditation using the CDs provided (varying from 10 to 30 minute guided meditations). You will be asked to keep a record of your home practice.
iv. You will be asked to notice how 'mindful' or in other words 'how present and aware you are in each moment' in the course of your normal everyday activities.

We need to know how you experience the MBSR programme so we will ask you some questions before the 8-week programme, during and two months after the programme ends (see C. below).

C. QUESTIONS ABOUT YOUR EXPERIENCE OF THE PROGRAMME:

i. Three face-to-face informal interviews lasting for 30-60 minutes with the study researcher at a time convenient to you to discuss your expectations of the mindfulness meditation programme (before you start) and your experiences of it at the end of the 8 week intervention and 2 months after you finish the 8 week programme.
ii. Monthly completion of standard questionnaires to let us know how you are feeling (e.g. depression, anxiety and stress).

You can stop participating at any time. Your decision to withdraw from the study will not affect your hospital treatment in any way.

Learning these MBSR techniques may help you become more aware of stress in your life and be able to cope with it more quickly and effectively.

7. Will you reimburse travels costs?

By taking part in this study you will be required to travel to the 8 weekly MBSR sessions, which will be based in Southampton. If you decide to take part in this study we will reimburse in full any costs you incur through travelling to the MBSR sessions.

8. What are the alternatives?

This study is aiming to determine the effectiveness of MBSR as a tool to manage depression and anxiety in prostate cancer patients undergoing active surveillance. However, whilst we are not offering any alternative forms of support for patients who don't want to undertake the MBSR programme, there are still many additional forms off support available to you as part of your standard care package. Should you feel that you would like additional support, your health care team will be able to assist you with this.

9. What are the risks of taking part in the MBSR programme?

There are no serious or non-reversible risks or side effects associated with the procedures included in this study.

Minor risks which might occur include:

You may feel frustrated during mindfulness practice because you may find that your mind wanders. You may also feel some minor stress due to the need to include mindfulness practice into your daily life. You may also experience some physical discomfort during sitting meditation and you will be encouraged to change position if this happens.

It is possible that you may be unable to do some of the gentle stretches that are part of several classes. These stretches are less strenuous than climbing up a flight of stairs and are not meant to increase strength or stamina. They are for the purpose of becoming aware of sensations in different parts of your body. You will be reminded not to stretch to the point of discomfort and alternative mindfulness activities will be available instead of the stretches if you are not able to participate in stretching for health reasons.

Another potential risk is the release of private information. To minimize the risk of releasing sensitive personal or family information, we have developed strict guidelines to protect privacy of medical and personal information.

Sometimes there may be feelings of sadness, anger, or anxiety associated with experiences that you may think about as you complete questionnaires or participate in training exercises. If talking or thinking about your experiences makes you unusually anxious, or if any part of the study process causes any bad feelings for you, you will be offered a referral to your GP who will be able to help you manage your distress. You will also be offered full access to the

Macmillan Cancer Information and Support Centre, based at Southampton General Hospital, which offers a free and confidential counselling service to patients. However, if at any time you find the interviews or questionnaires distressing, you are free to decline to answer any questions on the questionnaire or in the interviews. You also have the right to skip any questions.

For the reasons described above, the Mindfulness Instructor will observe you closely while participating in the programme described and, if you have any concerns, will notify the Researcher immediately. Mr Phil Russell (the Instructor) can be contacted by phone on (023 9225 0001) for more information or to discuss any concerns you may have about risks and side effects or any questions during the programme.

You may also feel annoyance at having to have blood samples collected from them. You will be reminded that you do not have to have you blood samples taken and that if you don't you are still free to take part in the 8-week MBSR programme.

10. What are the possible disadvantages of taking part?

There are no known disadvantages in taking part in the MBSR study, except for the time that you will be asked to commit.

11. What are the possible benefits of taking part?

If you agree to take part in this study, there may or may not be direct medical benefit to you. Benefits may include having more energy, more positive mood, and decreased feelings of stress. We hope the information learned from this study will benefit other people with prostate cancer in the future.

12. What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your researcher will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw your care will remain the same with your oncologist. If you decide to continue in the study you will be asked to sign an updated consent form. Also, on receiving new information, the study team might consider it to be in your best interests to withdraw you from the study.

13. What if something goes wrong?

If you have any concerns or complaints about any aspects of how this research has been conducted by the researcher then please contact, Dr Martina Prude, Research Governance Manager, University of Southampton, Room 4009, Legal Services, Building 37, Highfield, Southampton, SO17 1BJ. Telephone: 023 8059 8848/9 or email: mad4@soton.ac.uk

14. Will my taking part in the study be kept confidential?

Information produced by this study will be stored in the Researcher's locked file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate secure location. It is normal for study data to be transferred to computer and it is important that this transfer is carried out accurately. Confidentiality is always assured and your name and address is not transferred to computer with the data. In the storage of information there will be full adherence to the current Data Protection Act. Information contained in your records with your name on it may not be given to anyone not connected with the study without your written consent. Please also note that the researcher has a responsibility to report any disclosure by study participants during the study that clearly indicate malpractice or illegal activity.

All data will be stored in accordance with research governance for 10 years.

15. What will happen to the results of the research study?

The results of the research will be published in a medical book or journal and used for teaching purposes. When the study is completed, there will be copies of the published results available from Dr Geraldine Leydon (gerry@soton.ac.uk; 023 8024 1048) and Dr Brian Birch (brian.birch@suht.swest.nhs.uk; 023 8079 5165). Please note that your name nor any identifying information will be used in any publication or teaching materials without your specific permission.

16. Who is organising and funding the research?

The research is being funded by the National Institute of Health Research National School of Primary Care Research (NSPCR) and organised by the University of Southampton and Southampton University Hospital Trust (SUHT). The study is being conducted as part of the academic requirements of a PhD which is being overseen and managed by the University of Southampton's School of Medicine. The Researcher who is undertaking the PhD is an employee of the University of Southampton, the research team are University based and the Instructor is being paid by the NIHR. No-one is being paid for including you in this study.

17. Who has reviewed this study?

This research has been reviewed and given a favourable ethical opinion for conduct by the South Central – Oxford A Research Ethics Committee.

17. Contact for further information

If you have any questions regarding your rights as a participant in this research and/or concerns about the study, or if you feel under any pressure to enrol or continue to participate in this study, you may contact the study team – (local contact info to be added).

You may ask more questions about this study at any time. To do so, please contact Prof George Lewith (gl3@soton.ac.uk; 023 8024 1048).

Thank you again for reading this information and for considering participation in this study.

PATIENT INVITATION LETTER

[Southampton University Headed Paper]

TO A UNIVERSITY OF SOUTHAMPTON RESEARCH PROJECT

Project Title: Understanding Depression and Anxiety in Prostate Cancer: A feasibility study and evaluation of Mindfulness Based Stress Reduction (MBSR) for the management of depression and anxiety in prostate cancer patients undergoing active surveillance.

This prostate cancer clinic is participating in the above study which will test the use of an accepted type of relaxation / meditation technique.

The aim of the study is to find out whether we can help patients feel less depressed and anxious and have an improved sense of well-being.

The study will involve a few different activities over a 4 month period.

Your participation would involve:

1. 8-week relaxation / meditation course, including some home practice.
2. Keeping a record of your home practice during the course.
3. 3 informal interviews about your thoughts / experiences of the course.
4. Filling out brief questionnaires about your depression and anxiety and well-being before, during and after the course.

It is important for you to know:

5. Whether or not you take part, your routine care will not be affected.
6. The study will involve you taking part in 1-4 above.
7. It is entirely up to you if you wish to take part.

Attached to this letter, I have provided more details for you to read. If you think you might be interested in helping with this research please read the information on page 2 and follow the instructions provided.

Many thanks for your time.

With best wishes

Dr Brian Birch
Consultant Urologist

Project Title: Understanding Depression and Anxiety in Prostate Cancer: A feasibility study and evaluation of Mindfulness Based Stress Reduction (MBSR) for the management of depression and anxiety in prostate cancer patients undergoing active surveillance.

More details of the study

It is hoped that the study will lead to a better understanding of relaxation / meditation and its beneficial effects on reducing depression and anxiety in patients with prostate cancer.

Whatever you decide, **your medical or legal rights will not be affected** in any way. Your personal details have not been given to the researchers and it is up to you if you decide to take part in this study. **Your future care will not be influenced in any way by your decision.**

Enclosed you will find a **Patient Information Sheet** and a **Patient Reply Slip** provided by the researchers and a **freepost envelope**. The information sheet describes the study in greater detail. It also includes the researcher's telephone number if you have any questions about the study.

Instruction: for you to do

If you think you might be interested in hearing more **please read the Patient Information Sheet.** *Then please* **post your completed reply slip** *in the FREEPOST envelope. The reply slips allow you to:*

1. **Provide your contact details for the researcher**
   OR
2. **Say that you do not wish to take part and why**

The researchers would find it useful to know your reasons for not wishing to take part.

The Isle of Wight, Portsmouth and South East Hampshire Research Ethics Committee has reviewed this study and raised no objections on ethical grounds.

Many thanks for taking the time to read this letter.

With best wishes,

Dr. Brian Birch
Consultant Urologist

PATIENT REPLY SLIP

Your Name_____	**PLEASE TICK**
I WOULD like to hear more about the study and am happy to be contacted **If you would like to hear more please complete below fully:** Date of birth:_____/_____/_____ Email address: _____ Address: Contact telephone numbers: _____ _____ _____ _____ _____ _____ _____ _____ Post code _____ _____ Name of GP:_____	
OR I WOULD NOT like to hear more about the study	

MY REASON(s) for not wanting to hear more / take part:

Dated:	_____ / _____ / _____

THANK YOU

PLEASE POST USING THE FREEPOST ENVELOPE PROVIDED

PATIENT CONSENT FORM

[Southampton University Headed Paper]

Project Title: Understanding Depression and Anxiety in Prostate Cancer: A feasibility study and evaluation of Mindfulness Based Stress Reduction (MBSR) for the management of depression and anxiety in prostate cancer patients undergoing active surveillance.

Name of Researchers: Professor George Lewith, Drs Brian Birch, Geraldine Leydon, Roz Gibbs; Mr Sam Watts and Mr Philip Russell.

Please initial box

1. I confirm that I have read and understand the information sheet dated 9th September 2011 (Version 2) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that sections of any of my medical notes may be looked at by responsible individuals who are part of the study team, or from regulatory authorities. I give permission for these individuals to have access to my medical records. ☐

4. I understand that the research team will notify my GP about my participation in the study. ☐

5. I agree for a copy of this consent form to be given to the research team at University of Southampton ☐

6. I agree that all interviews conducted as part of this study will be audio taped in full ☐

7. I agree that verbatim quotes from the interviews will be anonymously utilised in the write up and publication of the investigation. ☐

Name of participant Date Signature

Name of Person taking consent Date Signature

Please complete fully:

Date of birth:____/____/____

Contact telephone number:_____

_____

Address:

_____

_____

_____

Email address:

_____

Post code _____ _____

Name of GP:_____

Copies: 1 for participant; 1 for Investigator Site File; 1 to be kept with clinical notes;

1 for Southampton University Research Team

Appendix 13

Interview Study Patient Information Pack Contents

PATIENT INVITATION LETTER

[Southampton University Headed Paper]

TO A UNIVERSITY OF SOUTHAMPTON RESEARCH PROJECT

Project Title: Understanding Distress in Prostate Cancer: a feasibility study into the design and evaluation of a novel support intervention for managing distress in prostate cancer.

This prostate cancer clinic is participating in the above study which will aim to better understand the specific needs and requirements of prostate cancer patients and to try to understand the types of interventions men with prostate cancer would find useful to help them manage any distress they are experiencing.

Your participation would involve:

5. Completing a single informal interview with a member of our research team.

It is important for you to know:

8. Whether or not you take part, your routine care will not be affected.
9. The study will involve you taking part in a tape recorded interview
10. It is entirely up to you if you wish to take part.

Attached to this letter, I have provided more details for you to read. If you think you might be interested in helping with this research please read the information on page 2 and follow the instructions provided.

Many thanks for your time.

With best wishes

Dr Brian Birch
Consultant Urologist

Project Title: Understanding Distress in Prostate Cancer: a feasibility study into the design and evaluation of a novel psychological support intervention for managing distress in prostate cancer.

More details of the study

It is hoped that the study will lead to a better understanding of the specific needs of men living with prostate cancer and the types of interventions they may be willing to take part in to help them better manage any distress they are experiencing due to their diagnosis. It is hoped that the information obtained from these interviews will help in the future creation and trialling of a new support intervention that prostate cancer patients can use to help manage distress.

Whatever you decide, **your medical or legal rights will not be affected** in any way. Your personal details have not been given to the researchers and it is up to you if you decide to take part in this study. **Your future care will not be influenced in any way by your decision.**

Enclosed you will find a **Patient Information Sheet** and a **Patient Reply Slip** provided by the researchers and a **freepost envelope**. The information sheet describes the study in greater detail. It also includes the researcher's telephone number if you have any questions about the study.

Instruction: for you to do

If you think you might be interested in hearing more **please read the Patient Information Sheet.** *Then please* **post your completed reply slip** *in the FREEPOST envelope. The reply slips allow you to:*

3. **Provide your contact details for the researcher**

   OR

4. **Say that you do not wish to take part. If you are willing to explain, the researchers would find it useful to know your reasons for not wishing to take part**

The researchers would find it useful to know your reasons for not wishing to take part.

This research has been reviewed and given a favourable ethical opinion for conduct by the South Central – Oxford A Research Ethics Committee.

Many thanks for taking the time to read this letter.

With best wishes,

Dr. Brian Birch
Consultant Urologist

PATIENT REPLY SLIP

Your Name_____	**PLEASE TICK**
I WOULD like to hear more about the study and am happy to be contacted **If you would like to hear more please complete below fully:** Date of birth:_____/_____/_____ Address: _____ _____ _____ _____ Post code _____ _____ Email address: _____ Contact telephone numbers: _____ _____ _____ _____ Name of GP:_____	
OR I WOULD NOT like to hear more about the study	
MY REASON(s) for not wanting to hear more / take part:	

Dated:	_____ / _____ / _____

THANK YOU

PLEASE POST USING THE FREEPOST ENVELOPE PROVIDED

PATIENT CONSENT FORM

[Southampton University Headed Paper]

Project Title: Understanding Distress in Prostate Cancer: a feasibility study into the design and evaluation of a novel psychological support intervention for managing distress in prostate cancer.

Name of Researchers: Professor George Lewith, Drs Brian Birch, Geraldine Leydon, Roz Gibbs; Mr Sam Watts and Mr Philip Russell.

Please initial box

1. I confirm that I have read and understand the invitation sheet dated 21st March (Version 3) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that sections of any of my medical notes may be looked at by responsible individuals who are part of the study team, or from regulatory authorities. I give permission for these individuals to have access to my medical records. ☐

4. I agree for a copy of this consent form to be given to the research team at University of Southampton ☐

5. I agree that all interviews conducted as part of this study will be audio taped in full ☐

6. I agree that verbatim quotes from the interviews will be anonymously utilised in the write up and publication of the investigation. ☐

6. I consent to be contacted again by the current research team to hear more details about the future support intervention they hope to design. ☐

Appendix 14

Qualitative Interview REC Confirmation Letter

NHS
Health Research Authority

NRES Committee South Central - Oxford A

Bristol Research Ethics Committee Centre
Whitefriars
Level 3 Block B
Lewins Mead
Bristol
BS1 2NT

Tel: 01173421331
Fax: 01173420445

10 April 2012

Prof George Lewith
Professor of Health Research
University of Southampton
Primary Medical Care
Aldermoor Health Centre
Aldermoor Close
SO16 5ST

Dear Prof Lewith

Study title:	**Understanding depression and anxiety in prostate cancer: A feasibility study and qualitative evaluation of Mindfulness Based Stress Reduction (MBSR) for the management of depression and anxiety in men with prostate cancer undergoing active surveillance.**
REC reference:	**11/SC/0355**
Protocol number:	**1**
Amendment number:	**SA1**
Amendment date:	**22 March 2012**

The above amendment was reviewed at the meeting of the Sub-Committee held on 03 April 2012 by the Sub-Committee in correspondence.

Ethical opinion

The Committee Members approved the changes to take a step back and interview 20-30 PCa patients to gather more information about their specific needs as PCa patients, whether they feel they would benefit from a support intervention and if so the types of intervention they would find acceptable.

The Committee Members requested the following changes: -

1. Changes to the Participant Information Sheet (PIS):
    a. The reply slip point 2 currently reads "Say that you do not wish to take part and why." Please remove "and why": this cannot be a requirement.
    b. Strengthen the following sentence, "The researchers would find it useful" to make it an invitation, such as "If you are willing to explain, the researchers would find it useful to know your reasons for not wishing to take part."
    c. Change the committee reviewing to South Central – Oxford A.

2. Changes to the Consent Form:
    a. Add a box for initialling to point 2.
    b. Remove point 4: it is not necessary to contact the GP for this interview.

Appendix 15: Qualitative Interview Guide

Project Title: Managing Distress in Prostate Cancer

Before beginning the interview you will need to:

- *Introduce yourself.*
- *Explain the purpose for conducting the interview,*
- *Explain how the interview will be structured (it is semi-structured, so there are specific questions to answer but they should also feel free to explore broader themes).*
- *Confirm with the participant that they have signed the consent form and double check that they are happy for the interview to be anonymously recorded.*
- *Reiterate that they can stop the interview at any time for a break, can ask for the recorder to be switched off or can in fact terminate the interview at any time without reason.*
- *Check if the participant has any questions before beginning.*

Opening Questions

1. Can you please describe how this all started and how you came to be diagnosed with prostate cancer in the first place?

2. Can you please tell me about your cancer and how it has affected you?

Probe: Mentally and physically

When initially diagnosed

What was life like before diagnosis

Unanswered questions

Active Surveillance

1. What does AS mean to you?

2. How was the concept of AS explained to you?

Probe: When?
Who by?
Adequate?
Questions left unanswered?
Other treatment options discussed?

3. Can you walk me through the information about AS that was available to you when you were first discussing it as a treatment option?

4. Thinking back was there some additional information you would have liked from your clinical care team about the use of AS.

5. Are you happy with being managed with AS and if you could go back would you select it again?

6. If you had to state one word that you associate with AS, what would it be?

Distress

1. Have there been moments on your cancer journey that you have found more distressing that others? Can you tell me about these?

Probe: Immediately after diagnosis

Start of treatment

Around the time of clinical tests

Now

2. What do you feel was/is the primary cause of your distress at these times?

Probe: Shock of diagnosis

Active surveillance

Any other issues?

3. In what ways, if at all, has being treated with AS caused you any distress?

4. Did you seek any support to help address your distress?

Probe: If not why not

If yes, what did you do? Did it help? How?

5. Thinking about the times you experienced distress, what kind of support would have allowed you to have better managed this distress?

Probe: Emotional support

Informational support

Educational support

6. Would you be likely to attend a PCa specific support group?

Probe: Comfortable in front of 8-10 other men

Travel demands

Time demand

Work commitments

Tailoring Support to Suit Men with PCa being Managed with AS

1. We are trying to design a support intervention for PCa patients. One component of this may be group support. What are you views on group based support?

2. Thinking about a group support programme, what would it look like to you in terms of the number of sessions, length of each session, group size etc?

Probe: Group setting

Group leader gender

Group leader background – CNS/lay person/expert patients…?

Number of sessions

Length of sessions

3. If you had access to such a group support programme, do you think you would attend?

Probe: If so, why

If not, why not?

4. Another component of the support intervention may be an internet based support service for PCa patients that would provide you with information specific to your illness and treatment. Is this something you would find helpful and would use?

Probe: Do you currently use the internet?

What aspects of their illness and treatment decisions would you use it for?

Why do you think/not think it would be helpful

Would you use it?

5. If we create the internet support service, would you think there would be value in creating a booklet based hard copy as well?

Probe: For patients without internet access.

Conclusion

1. Are there any other relevant issues we haven't covered that you would like to mention or discuss?

2. Are there any questions that you would like to ask me?

Debrief

Thank you very much for taking the time to speak with me. Your participation is very much appreciated. I want to remind you that although our conversation will be typed up, all identifying information will be removed from the typed up interview so that if someone heard or read your interview they would not know who you are.

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