

STRESS, SYMPTOMS, SYMPTOM DISTRESS, AND SYMPTOM  
SELF-MANAGEMENT IN LOCALIZED PROSTATE CANCER

By

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## ABSTRACT

Prostate cancer is the most commonly diagnosed cancer and second leading cause of death in American men. Patients with localized prostate cancer may experience unique and multidimensional symptoms that are distressful from treatment and thereafter. This cross-sectional correlational study aimed to investigate the relationships among stress, symptoms, symptom distress, and symptom self-management and identify the effective strategies of symptom self-management in men with localized prostate cancer following prostatectomy or radiation therapy.

Eight saliva samples and 3 questionnaires (Perceived Stress Scale, Symptom Indexes, and Strategy and Effectiveness of Symptom Self-Management) were obtained from each participant between 1 and 3 months following their first prostate cancer treatment. The sample consisted of 53 men with localized prostate cancer. Mean salivary cortisol concentrations for the entire sample ranged from 0.3 to 0.08 ug/dL. Cortisol was secreted in a circadian rhythm with heightened activity in the early morning and lowered activity late in the day. The circadian pattern of cortisol secretion was similar in both the prostatectomy and radiation therapy groups, although the values were slightly different. Two areas Under the Curve (*AUC*) of salivary cortisol were calculated. Three cortisol circadian rhythms were identified, but the majority of the sample had a typical negative consistent circadian rhythm.

Patients with localized prostate cancer who underwent radical prostatectomy or radiation therapy had low perceived stress. Perceived stress was positively correlated with  $AUC_G$ , noon salivary cortisol concentrations, and afternoon salivary cortisol

concentrations. Subjects reported a moderate degree of symptoms and symptom distress on urinary, bowel, and sexual dysfunction 1-3 months following treatments. The most effective strategies of urinary symptom management were pad and kegel exercise; the most effective strategy of bowel symptom management was rest or endure; the most effective strategies of sexual dysfunction management included express their feelings or find alternative ways to express their affection. The symptom self-management strategies were significantly and positively correlated with symptom self-management effectiveness.

Symptom distress and  $AUC_G$  were significant and strong predictors of symptom self-management. Findings can help health care providers develop effective strategies for symptom self-management that enhance health related quality of life among men with localized prostate cancer.



## CHAPTER I

### INTRODUCTION

Prostate cancer is the sixth most common cancer worldwide. In the United States, prostate cancer is the most commonly diagnosed non-skin cancer and the second leading cause of death among men. In 2008, approximately 186,320 American men will be diagnosed with prostate cancer and about 28,660 men will die from the disease ("American Cancer Society Facts and Figures," 2008; Jemal et al., 2008). Current estimates are that every nineteen minutes a man dies from prostate cancer and almost one in every six (17%) males in the United States will experience prostate cancer in his lifetime ("American Cancer Society Facts and Figures," 2008; Foundation, 2008). However, five-year survival rates have steadily improved since 1974, and the overall relative 5-year survival for prostate cancer is 98 % across all races and cancer stages in the United States("American Cancer Society Facts and Figures," 2008; Foundation, 2008).

Approximately 90 % of all prostate cancers are detected in the local and regional stage. Many men have clinically localized prostate cancer which consists of low grade tumors that do not extend beyond the prostate gland (Eton, Lepore, & Helgeson, 2001; Foundation, 2008). Patients with clinically localized prostate cancer may experience unique and multidimensional symptoms that are distressful from diagnosis through treatment and thereafter. These symptoms are in the form of physical and psychological sequelae associated with the disease and treatments (Eton et al., 2001; Foundation, 2008; O'Rourke, 2004; Wallace & Powel, 2002).

The physical and psychological symptoms associated with the disease and treatments may result in symptom related distress which has the potential to alter quality of life through alterations in self care, physical functioning, symptom management, and treatment tolerance (Portenoy et al., 1994; Rhodes & McDaniel, 1999). When Hans Selye (1956) first proposed the concept of stress, he distinguished eustress from distress and defined distress as encompassing more severe, protracted, and uncontrollable situations (both physically and psychologically) (Selye, 1956). Furthermore, distress is associated with symptoms, and both distress and symptoms influence disease status (Shelby & McCance, 2001). For example, symptom-related distress in patients with cancer has been found to significantly and independently predict changes in physical functioning and performance status (Given, Given, Azzouz, & Stommel, 2001; Selye, 1979; Shelby & McCance, 2001). The occurrence of multiple symptoms in patients with prostate cancer has been shown to predict treatment failures and poor therapeutic outcomes (Clark, Inui et al., 2003; Harlan et al., 2001; Korfage et al., 2005).

Symptom distress has been negatively correlated with length of survival in patients with cancer (Goodell & Nail, 2005; McCorkle & Benoliel, 1983; McCorkle & Young, 1978; Portenoy et al., 1994). Interventions targeting symptom distress may change functional status, improve symptom self-management and quality of life, and influence patient outcomes including morbidity and mortality (Rhodes & McDaniel, 1999). Developing effective strategies for symptom self-management that ultimately enhance the quality of life in patients with localized prostate cancer requires an

understanding of how patients perceive their stress, experience their symptoms and symptom distress, and effectively manage their symptoms.

#### Statement of Problem

The prevalence of prostate cancer extends beyond the United States; it is one of the most common malignancies among men in Europe, Sweden, Japan, China, and Taiwan (Cancer, 2008; Curran et al., 1997). Prostate cancer, therefore is a public health problem throughout the world.

Due to the location of the prostate gland and the delicate nature of the treatment, patients with localized prostate cancer usually have problems with urinary incontinence and obstruction, bowel symptoms, and sexual functioning. These unique and distressful symptoms are the most common domains of health-related quality of life affected by the disease and its treatments (Abel, Dafoe-Lambie, Butler, & Merrick, 2003; Clark, Bokhour, Inui, Silliman, & Talcott, 2003; Clark & Talcott, 2001; Cooperberg, Park, & Carroll, 2004; Hernandez & Thompson, 2004; Michaelson et al., 2008).

Many studies have reported that physical function, psychological stress, complications/side effects, symptoms or symptom distress are related to disease stage and different treatments among men with prostate cancer (al-Abany et al., 2002; Bisson et al., 2002; Damber & Aus, 2008; Hernandez & Thompson, 2004; Michaelson et al., 2008). However, few studies have focused on the evidence-based practice or the interaction among salivary cortisol, perceived stress, symptoms, and symptom distress (Pruessner, Hellhammer, & Kirschbaum, 1999; Van Eck & Nicolson, 1994; Wright, Lin, Cowan, Carroll, & Litwin, 2008). Furthermore, there is little literature that supports effective

symptom self-management strategies and no study has investigated the relationships among stress, symptoms, symptom distress, and symptom self-management in men with localized prostate cancer following radical prostatectomy or radiation therapy was found previously.

### Purpose

The overall purpose of this study was twofold: (a) to investigate the relationships among stress, symptoms and symptom distress, and symptom self-management in patients with localized prostate cancer following radical prostatectomy or radiation therapy, and (b) to identify effective symptom self-management strategies among patients with localized prostate cancer following radical prostatectomy or radiation therapy.

The specific aims of the study and related research questions were:

**Aim One:** To examine physiological and psychological stress responses in men with localized prostate cancer following radical prostatectomy or radiation therapy. There were three research questions.

### Research Questions:

1-a. What are the levels and circadian patterns of the physiological stress response measured by salivary cortisol? Are there any differences between the 2 subgroups?

1-b. What are the levels of the psychological stress response as measured by the Perceived Stress Scale? Are there any differences between the 2 subgroups?

1-c. What is the relationship between the physiological stress response and the psychological stress response?

**Aim Two:** To describe the severity and frequency of symptoms and the degree of symptom distress experienced by men with localized prostate cancer following radical prostatectomy or radiation therapy. There were three research questions.

**Research Questions:**

2-a. What levels of symptoms (severity and frequency) do men with localized prostate cancer following radical prostatectomy or radiation therapy experience?

2-b. What is the degree of symptom distress among men with localized prostate cancer following radical prostatectomy or radiation therapy?

2-c. What is the relationship between symptoms and symptom distress among men with localized prostate cancer following radical prostatectomy or radiation therapy?

**Aim Three:** To describe symptom self-management strategies and their perceived effectiveness among men with localized prostate cancer following radical prostatectomy or radiation therapy. There were three research questions.

**Research Questions:**

3-a. What is the frequency of strategies for symptom self-management used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

3-b. What is the perceived effectiveness of strategies used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

3-c. What is the relationship between the frequency of using a strategy to alleviate symptoms and the perceived effectiveness of each strategy used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

**Aim Four:** To examine the relationships among stress (physiological and psychological responses), symptoms and symptom distress, and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy. There were five research questions.

**Research Questions:**

4-a. What are the relationships among stress, symptoms, symptom distress, and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy?

4-b. To what extent does stress (salivary cortisol and perceived stress) predict symptoms and symptom distress among patients with localized prostate cancer following radical prostatectomy or radiation therapy?

4-c. To what extent does stress (salivary cortisol and perceived stress) predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

4-d. To what extent do symptoms and symptom distress predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy and/or radiation?

4-e. To what extent do stress (salivary cortisol and perceived stress), symptoms, and symptom distress predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

### Significance to Nursing and Health Care

As discussed above, prostate cancer is the most commonly diagnosed non-skin cancer and the second leading cause of death in American men ("American Cancer Society Facts and Figures," 2008). Men suffering from prostate cancer can experience a wide range of distressful symptoms both physical and psychological that are associated with the disease and its treatment modalities (Hernandez & Thompson, 2004; Korfage, de Koning, Roobol, Schroder, & Essink-Bot, 2006; Michaelson et al., 2008).

It is known that stressful life events are a risk factor for cancer (Selye, 1979; Shelby & McCance, 2001). Stress also can influence an individual's disease status by modulating the immune response (Herbert & Cohen, 1993; Kiecolt-Glaser & Glaser, 1991). As defined previously, distress is related to severe, protracted, and uncontrollable psychological and physical situations, which can lead to disease states (Rhodes & Watson, 1987). Symptoms and symptom distress affect performance, self-care, and symptom management (McClement, Woodgate, & Degner, 1997; Rhodes & McDaniel, 1999). There is some evidence that stress reduction strategies may improve cancer survival, lower psychological stress, decrease the rate of cancer recurrence, and enhance the quality of life (Carlson, Speca, Patel, & Goodey, 2004). In addition, symptom self-management is associated with health related quality of life, physical functional status, and treatment tolerance in patients with cancer (Fu, LeMone, & McDaniel, 2004; Smith, Holcombe, & Stullenbarger, 1994).

This is the first study to focus on stress, symptoms and symptom distress and symptom self-management among men with localized prostate cancer following radical

prostatectomy or radiation therapy; and, specifically, to measure the levels of physiological stress response by using the biomarker salivary cortisol. In order to advance nursing practice, it is critical to develop effective interventions and symptom self-management strategies that are evidence-based. The findings of this prospective study have the potential to help health care providers enhance the effectiveness of nursing interventions for stress management and symptom self-management among men with localized prostate cancer. To develop comprehensive symptom self-management strategies and enhance the effectiveness of strategies, it is important to investigate stress, symptoms and symptom distress, and symptom self-management experienced by men with localized prostate cancer following radical prostatectomy and/or radiation therapy.

#### Summary

Men with localized prostate cancer may experience disease-specific symptoms (such as urinary incontinence, sexual dysfunction) and related symptom distress which can influence how they perceive and manage their symptoms. Little research has focused on stress, symptoms and symptom distress, and symptom self-management among men with localized prostate cancer. Therefore, the ultimate goal of this study was to identify the factors related to stress, symptoms, symptoms distress, and symptom self-management and provide evidence that would help health care providers develop effective self-management strategies that would improve health related quality of life among men with localized prostate cancer following radical prostatectomy or radiation therapy.



## CHAPTER II

### LITERATURE REVIEW

#### Introduction

Chapter II presents the Theory of Unpleasant Symptoms which was the theoretical framework for this study and guided the development of study conceptual framework. In addition to the theoretical and conceptual frameworks, the theoretical and operational definitions of each study variable including physiological stress response, psychological stress response, symptoms, symptom distress, and symptom self-management are described. An integrated literature throughout the chapter is a review of published literature related to prostate cancer, stress, symptoms, symptom distress, symptom self-management, and relationships among these concepts.

#### The Theory of Unpleasant Symptoms (TOUS)

The Theory of Unpleasant Symptoms (TOUS) was originally developed by Lenz, Pugh, Milligan, Gift, and Suppe in 1995 (Lenz, Suppe, Gift, Pugh, & Milligan, 1995). In order to make the model of unpleasant symptoms less linear and reflect the dynamics of clinical situations, the authors revised the TOUS in 1997 (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). The theory focuses on the symptom experience, with multiple symptoms occurring together, rather than one symptom in isolation. TOUS is based on the assumption that sufficient commonalities exist among symptoms. The theory uniquely implies that the management of one symptom will contribute to the management of other symptoms. TOUS therefore addresses the synchronic occurrence of more than one

symptom that may exert a multiplicative effect on symptom experience, distress, and performance (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

TOUS has three components: 1) the symptoms that the individual is experiencing, 2) the influencing factors that give rise to or affect the nature of the symptom experience, and 3) the consequences of the symptom experiences. Physiological, psychological, and situational factors are antecedent factors which influence the symptom experience. The consequence of symptoms is performance which includes functional and cognitive activities (Fu et al., 2004; Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

### Symptoms

Symptoms are the central focus of the TOUS. Symptoms are defined as perceived indicators of change in normal functioning as experienced by patients. Symptoms can be considered alone or combination. They are seen as multiplicative, rather than additive. In the original model of the TOUS (Figure1), one symptom is depicted and it is a purely linear model. The updated model of the TOUS (Figure2) proposes that symptoms can occur alone or in isolation from one another but that, more often, multiple symptoms are experienced simultaneously. The revised model also reflects more interaction among key components (symptoms, influencing factors, and outcomes) (Lenz et al., 1997; Lenz et al., 1995). Multiple symptoms can occur together as a result of a single event; for example, surgery or one symptom can precede another such as fatigue proceeding depression.

Each symptom is conceptualized to be a multidimensional experience, which can be conceptualized and measured separately or in combination with other symptoms.

Symptoms have the dimensions of intensity (severity), timing (frequency, duration, and relationship to events), distress (the person's reaction to the sensation), and quality (descriptors used to characterize the symptom, location of the symptom, or response to intervention). Intensity refers to the severity, strength, or amount of the symptom being experienced. The time dimension includes the frequency with which an intermittent symptom occurs, the duration of a persistent symptom, or a combination of frequency and duration of symptoms. The symptoms can be intermittent but persist over long periods of time or chronic but varying in intensity. The distress dimension of the symptom experience refers to the degree to which the person is bothered by the symptom(s). Symptoms can vary in their quality or the way they are manifested. The quality of a symptom can include description of the location of a given sensation, as well as the degree to which a patient responds to a particular intervention (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

#### Influencing Factors/Antecedents of the Symptom Experience

It is proposed that three categories of influential factors, physiological, psychological, and environmental/situational affect one's predisposition to or manifestation of a given unpleasant symptom experience. The influencing factors are also the antecedents of the symptom experience in the TOUS. Physiological factors are often reflected in unpleasant symptoms associated with alterations in the normal functioning of bodily systems or the existence of any pathology. Physiological antecedents commonly characterize the severity of the disease, such as comorbidities, abnormal laboratory findings or other pathological findings (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

Examples of physiological factors include the mechanisms of head injury, the individual's immunity and defense functioning, or physiological response to stress (i.e. the level of stress hormone).

The psychological factors that are antecedents include the individual's mental state or mood (depression), affective reaction to illness (mood status), psychological response to stress (the degree of perceived stress or the level of anxiety) and degree of uncertainty and knowledge about the symptoms and their possible meaning (perception of illness experience or symptom experience). Situational/environmental antecedents include aspects of the social and physical environment that may affect the individual's experience and reporting of symptoms (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995). Examples of situational/environmental factors include social support, marital status, and resources or any situational events that may influence symptom experience.

#### Relationships among Influential Factors

In the original model of the TOUS (Figure1), influential factors are depicted exerting a unidirectional influence on the symptom experience, and not related to one another. In the updated model of the TOUS (Figure2), some improvements have been made to more accurately depict these relationships. First, the three types of influential factors are related to one another over and above their individual relationships to symptoms. Second, the model asserts that physiological, psychological, and situational factors can interact with one another in their relation to symptoms (Lenz et al., 1997; Lenz et al., 1995).

### Outcomes/Consequences of the Symptom Experience

Outcome or consequence of the symptom experience is the final component of the theory of unpleasant symptoms. Performance is conceptualized to include functional status or performance, cognitive functioning, and physical performance. Functional performance is conceptualized broadly to include physical activity, activities of daily living (ADLs), social activities and interaction, and role performance including work and other role-related tasks. Cognitive performance includes concentrating, thinking, and problem-solving. Performance is affected by the level and nature of the symptom experience (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

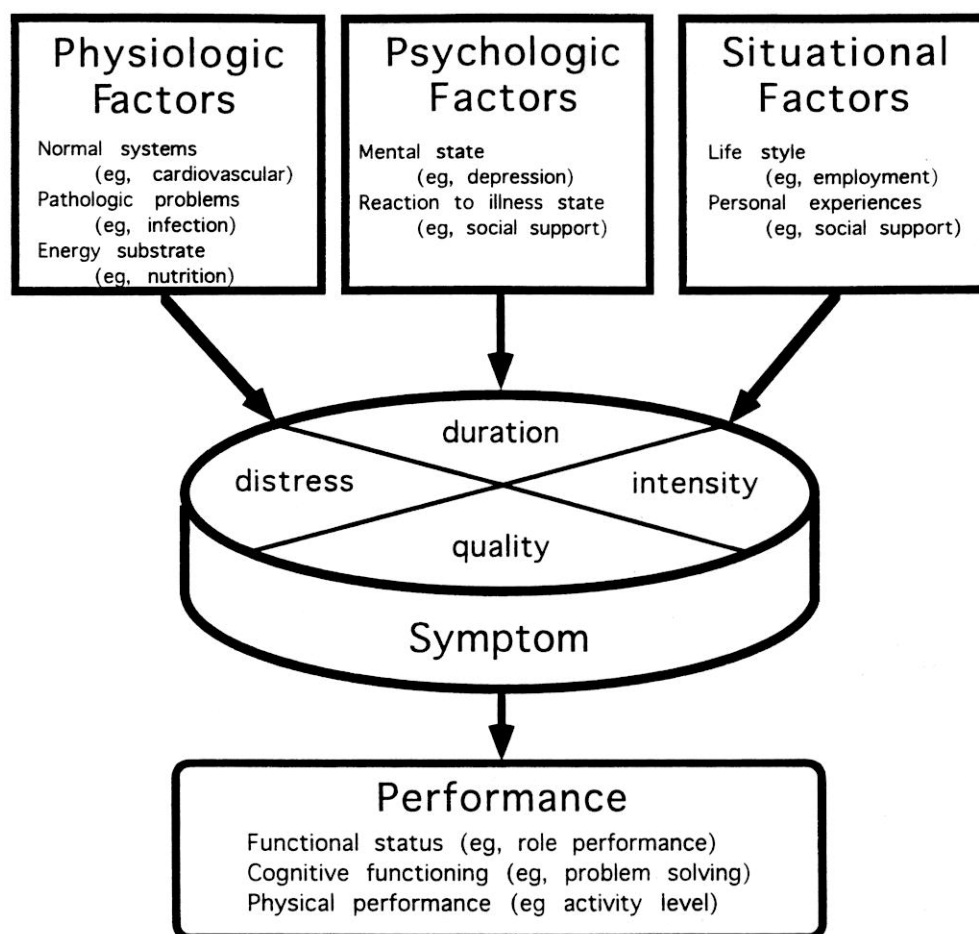
### Relationships among the Three Major Components

Compared to the original TOUS model (Figure 1), the revised TOUS model more accurately depicts the relationships among symptom experiences, influential factors and outcomes (Figure 2). First, the revised TOUS model depicts reciprocal relationships among central concepts (influential/antecedent factors, symptom experience, and outcomes/consequences). Second, the experience of unpleasant symptoms can change one's physiological, psychological, and situational status. For example, individuals with chronic fatigue may experience increased mood disturbance.

Third, the revised TOUS model proposes that outcomes (performance) have a reciprocal relation with the symptom experience. The revised model also posits that decreased levels of performance can have a negative feedback loop to the influential factors (physiological, psychological, and situational factors). Additionally, antecedents/influential factors can have an interaction effect in their relation to the symptom

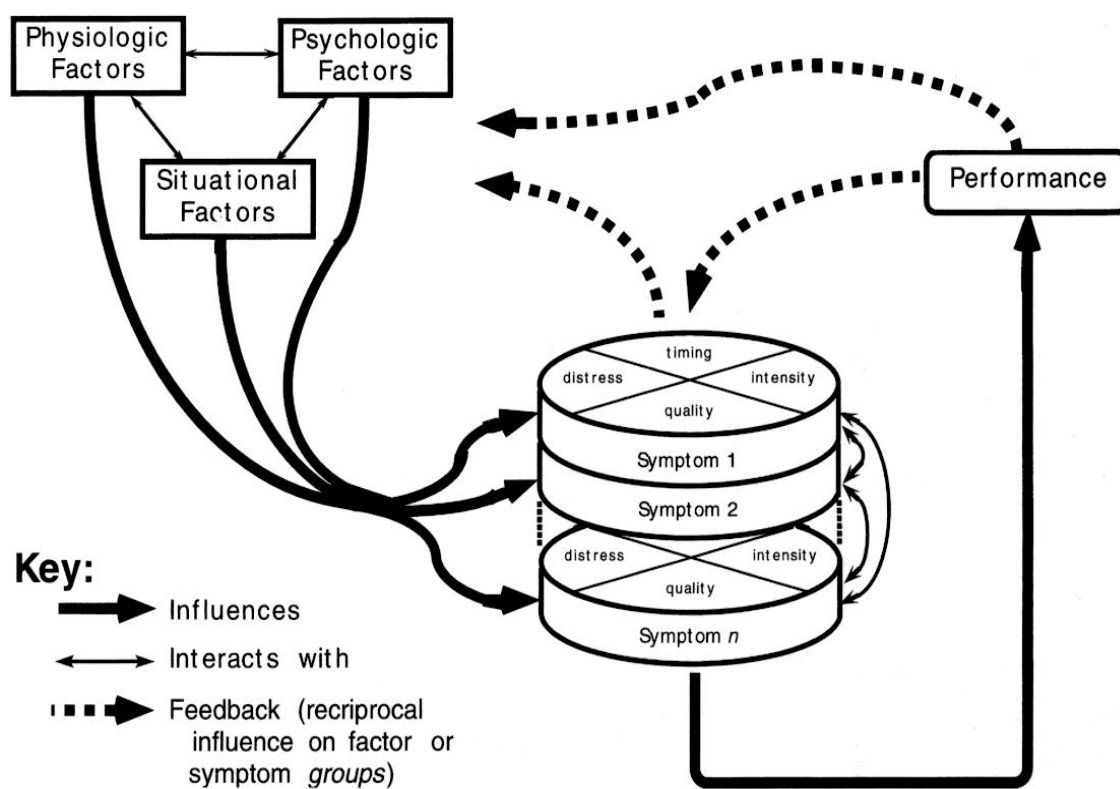
experience. Furthermore, the symptom experience can have a moderating or mediating influence on the relationship between influential factors and outcomes/performance (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

Figure 1.

*The Original Middle-Range Theory of Unpleasant Symptoms*

From: Reprinted with permission from Lenz, ER, Supp F, Gift AG, Pugh LC, Milligan RA. Collaborative development of middle-range nursing theories: toward a theory of unpleasant symptoms. *Adv Nurs Pract.* 1995; 17(3):1-13. © 1995, Aspen Publishers

Figure 2.

*The Updated Middle-Range Theory of Unpleasant Symptoms*

From: Lenz: ANS Adv Nur Sci, Volume 19(3). March 1997.14-27



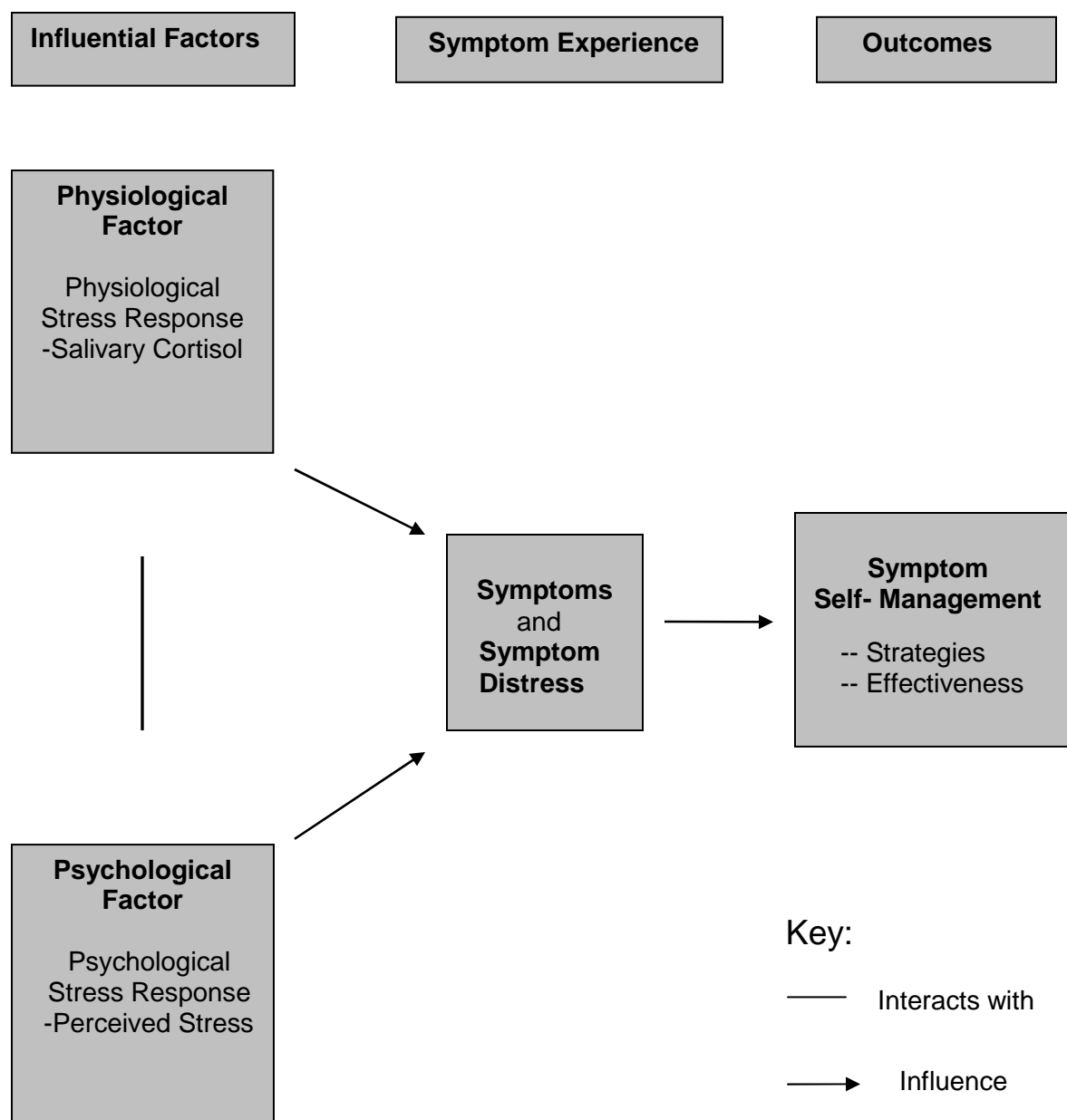
### Conceptual Framework

The main concepts of this study included stress, symptoms, symptom distress, and symptom self-management. After reviewing the relevant theories and theoretical frameworks among stress, symptoms, symptom distress, and symptom management, the updated Theory of Unpleasant Symptoms was identified as a middle-range theory which focused on symptoms and patient's performance; therefore it was chosen to guide the development of conceptual framework for this study.

The conceptual framework for this study was comprised of three key components: antecedent/influential factors, symptom experience, and consequences/outcomes. Influential factors were categorized into physiological and psychological factors. The physiological factor was represented by the physiological stress response and the psychological factor was represented by the psychological stress response. The symptom experience was represented by symptoms and symptom distress. The outcomes were represented by symptom self-management which included strategies and their effectiveness. Figure 3 depicts the conceptual framework of the relationships among stress, symptoms, symptom distress, and symptom self-management.

Figure 3.

*The Relationships among Stress, Symptoms, Symptom Distress, and Symptom Self-Management*



### Antecedents/Influential Factors

Antecedents are those events or incidents that occur prior to the occurrence of the concept (Walker & Avant, 1995). Influential factors are the events which influence the concept. Antecedent factors are the influential factors in the conceptual framework of this study.

In the conceptual framework for this study, there were two influential factors, physiological and psychological that influence symptom experience and outcomes in men with localized prostate cancer. The physiological factor was represented by the physiological stress response, specifically the levels of salivary cortisol; and the psychological factor was represented by psychological stress response, specifically the degree of perceived stress. Physiological and psychological stress responses directly influenced symptoms and symptom distress, and indirectly affected symptom self-management through symptoms and symptom distress among men treated with localized prostate cancer. In addition, the physiological stress response and psychological stress response were associated with each other.

### Symptom Experience

Symptom experience is comprised of symptoms and symptom distress and was the central focus of this conceptual framework. Symptoms were defined as perceived indicators of change in normal functioning as experienced by men with localized prostate cancer following radical prostatectomy and/or radiation therapy. Symptoms were conceptualized to be multidimensional, subjective and personal experience (Lenz et al., 1997). Symptom distress was one of the dimensions of symptoms. Symptom distress was

defined as physical or mental anguish, the degree of discomfort, or suffering that results from the specific symptom the patients perceived to experience or the patient's reaction to the sensation (Lenz et al., 1997; McCorkle & Young, 1978). Other dimensions of the symptoms include the intensity (severity), the timing (frequency or duration), and the quality (location of the symptom) (Lenz et al., 1997; McDaniel & Rhodes, 1995).

#### Consequences/Outcomes

Consequences or outcomes are those events or incidents that occur as a result of the occurrence of the concept (Walker & Avant, 1995). Symptom self-management was the outcome/consequence in the conceptual framework. Symptom self-management included the frequency of symptom self-management strategies and the effectiveness of the symptom self-management strategies patients with localized prostate cancer following radical prostatectomy or radiation therapy used.

#### Relationships among Influential Factors, Symptom Experience, and Outcomes

Stress, symptoms, symptom distress, and symptom self-management were the key concepts in the conceptual framework. According to the updated Theory of Unpleasant Symptoms, relationships among these key components were reciprocal and hypothesized to be related to one another. In the conceptual framework, stress, symptoms, symptom distress, and symptom self-management were associated with each other. Salivary cortisol and perceived stress were physiological and psychological influential factors and directly influenced the symptoms and symptom distress; the influential factors also had an indirect effect on symptom self-management through symptoms and symptom distress.

In addition, symptoms and symptom distress also directly influenced symptom self-management. Furthermore, symptoms and symptom distress were proposed to mediate the interaction between influencing factors (physiological and psychological stress responses), and outcomes (symptom self-management) based on the updated Unpleasant Symptoms Theory.

## Theoretical and Operational Definitions

### Stress

*Theoretical Definition:* Stress was defined as a nonspecific response of the body to any demand; stress was the body's biological response to a perceived emotional or physical threat. Regardless of the cause, situational context, or psychological interpretation of a demanding situation, the stress response involved the same chain of events and the same pattern of physiological correlates (Selye, 1946, 1956, 1973).

*Operational Definition:* Stress consisted of the biological/physiological and psychological stress responses. The physiological stress response was measured by the levels and circadian pattern of saliva cortisol in men with localized prostate cancer 1-3 months following radical prostatectomy or radiation therapy.

The psychological stress response was represented by perceived stress. It was measured by the Perceived Stress Scale (Perceived Stress Scale, PSS) to discover how men treated with localized prostate cancer perceived or evaluated as stressful or not stressful their treatment modalities, symptoms, and symptom distress 1-3 months after their first treatment.

### Symptoms

*Theoretical Definition:* Symptom was conceptualized as a subjective phenomenon which an individual regards as an indication or characteristic of a condition departing from normal function, sensation, or appearance. A symptom was an experience that was perceived and verified only by the individual experiencing the phenomenon; therefore, a symptom was subjective and experiential (Fu et al., 2004). Symptoms were

conceptualized to be a multidimensional experience of intensity (severity), timing (frequency, duration, and relationship to events), distress (the person's reaction to the sensation), and quality (descriptors used to characterize the symptom, location of the symptom, or response to intervention) (Gift, 2004; Lenz et al., 1997; Lenz et al., 1995).

*Operational Definition:* This study measured symptoms experienced by men treated with localized prostate cancer 1-3 months after their first treatment. Symptoms measured in this study included urinary problems (urinary incontinence and obstruction), sexual dysfunction, and bowel problems. In this study, symptoms were measured by the Symptom Indexes which included 4 dimensions (severity/intensity, frequency/duration, quality, and distress) of the symptoms (urinary problems, sexual dysfunction, and bowel problems).

### Symptom Distress

*Theoretical Definition:* Symptom distress was defined as physical or mental anguish, the degree of discomfort, or suffering that results from the specific symptom the patient perceived to experience (McCorkle & Young, 1978; Rhodes & Watson, 1987).

*Operational Definition:* Symptom distress was defined as the degree of distress, bother, or worry from the symptom associated with urinary problems (urinary incontinence and obstruction), sexual dysfunction, and bowel problems experienced by men with localized prostate cancer 1-3 months following radical prostatectomy or radiation therapy. In this study symptom distress was measured by the Symptom Indexes.

### Symptom Self-Management

*Theoretical Definition:* A theoretical definition of symptom self-management was not found in the literature. Symptom management was defined as a dynamic and multidimensional process in which patients intentionally and purposefully act on and interact with their perceived symptom (or previous perception) to initiate activities or direct others to perform activities to relieve or decrease distress from and prevent the occurrence of a symptom (Fu et al., 2004). Symptom management has been conceptualized as self-care or self-management. Self-management is defined as “the application of skill or care in the manipulation, use, treatment, or control (of things or persons) by oneself; or in the conduct of something by oneself” (University, 2005). Symptom self-management was defined by the author in this study as the application of strategies the individual (patients) used to intentionally alleviate the symptom (s) and to improve the quality of life.

*Operational Definition:* In this study symptom self-management included the strategies of symptom self-management and the effectiveness of strategies used to alleviate symptoms of urinary, bowel, and sexual dysfunction among patients treated with localized prostate cancer. Symptom self-management was measured by the Strategy and Effectiveness of Symptom Self-Management Questionnaire (SESSM). The SESSM questionnaire measured 1) the frequency of symptom self-management strategies, and 2) the effectiveness of strategies used by men with localized prostate cancer following radical prostatectomy or radiation therapy. In addition to self-management strategies that



are listed in the Questionnaire, participants could add the strategies they used to manage their symptoms.

## Literature Review

No reported studies of stress, symptoms, symptom distress, and symptom self-management in men with localized prostate cancer were found in the literature. This literature review summarizes findings from relevant studies that included the concepts of stress, symptoms, symptom distress, or symptom self-management. In addition to an integrated literature review, an introduction to localized prostate cancer is presented.

## Localized Prostate Cancer

Prostate cancer is the most frequent cancer among men in the United States, northern and western Europe, and part of Asia (Japan, China, and Taiwan) ("American Cancer Society Facts and Figures," 2008; Bracarda et al., 2005; Cancer, 2008). Early detection of prostate cancer has increased because of the introduction of prostate specific antigen (PSA) screening in the United State since the late 1980s. Due to early detection and diagnosis, the 5-year overall relative survival rate for prostate cancer has increased from 79.6 % to 98 % since 1983 (Bracarda et al., 2005; Foundation, 2008; Moul et al., 2003; Zeller, 2008). Approximately 90 % of all prostate cancers are detected in the local and regional stage; the cure rate for prostate cancer is nearly 100% in men diagnosed at an early stage of the disease. The five-year disease-free survival is estimated to be 99 % for localized prostate cancer across all races (Damber & Aus, 2008; Foundation, 2008; Miller et al., 2007).

The diagnosis of prostate cancer is definitively established by biopsy. The stage of the disease determines the appropriate type of therapy. There are three anatomic systems commonly used to classify prostate cancer in the United States: 1. the Jewett

system and the American Joint Committee on Cancer (AJCC) (stage A-D), 2. the International Union Against Cancer (UICC) (TNM— tumor, node, metastasis), 3. the World Health Organization (WHO) grading of prostate tumors according to the level of cellular differentiation noted in the biopsy (Bracarda et al., 2005; Hernandez & Thompson, 2004; O'Rourke, 2004; Wallace & Powel, 2002).

The most common system used for grading prostate cancer is the Gleason score. The Gleason grading system involves rating cancerous prostate tissue from 1 to 5; scores are based on how much the arrangement of the cancer cells mimics glandular tissue. Two grades are assigned to the most common patterns of cells that appear; these two grades (they can be the same or different) are then added together to determine the Gleason score (a number from 1 to 10) (Hernandez & Thompson, 2004; O'Rourke, 2004).

Clinical staging is based primarily on the presence or absence of a prostatic nodule on the digital rectal examination (DRE). Tumors with a Gleason score of 7 or greater are the most aggressive. Men with untreated tumors, based on a core-biopsy or a needle-aspiration-biopsy specimen, classified as localized ( $T_1$ - $T_2$ ,  $N_0$ ,  $M_0$ ), having a Gleason score less than 6, and with a grade 1 or 2 according to the WHO criteria have less aggressive tumors. The staging procedures of prostate cancer derive from the bioptic diagnosis of the disease (i.e. transrectal ultrasound and prostate-specific antigen, PSA) and traditional imaging techniques (i.e. chest X-ray, abdomen CT or MRI) (Bracarda et al., 2005; Hernandez & Thompson, 2004; Rosenfeld, Roth, Gandhi, & Penson, 2004).

Treatments are determined by stage and grade of disease at diagnosis, prostate-specific antigen (PSA) levels and the results of DRE, along with age at diagnosis,

functional status and life expectancy (Damber & Aus, 2008; Harlan et al., 2001). There is no one best treatment for men with localized prostate cancer. The selection of treatment is based on factors other than survival advantage, such as the effect of therapy on health-related quality of life (Eton & Lepore, 2002; Harlan et al., 2001). Treatment options for localized prostate cancer include watchful waiting/expectant management, radical prostatectomy, whole prostate radiation therapy (external beam radiation therapy, interstitial brachytherapy, radioactive seed implantation), and cryotherapy. Neoadjuvant hormone therapy is sometimes offered before radiation therapy or surgery treatments (Damber & Aus, 2008; Hernandez & Thompson, 2004). The most frequently used approaches to localized prostate cancer are watchful waiting, external radiation therapy and radical prostatectomy; prostatectomy and radiation therapy are the most common treatments for men with early stage prostate cancer (Michaelson et al., 2008).

Watchful waiting is an acceptable alternative for men with low-grade, clinically localized disease and a life expectancy of 10 years (O'Rourke, 2004). Radical prostatectomy is performed through a retropubic approach, and it provides excellent cancer control for patients with localized prostate cancer (Hernandez & Thompson, 2004). Radiotherapy can sterilize prostate tumors and the higher the radiation therapy dose administered, the greater the likelihood of obtaining local control (al-Abany et al., 2002). There is lack of consensus among physicians about the relative outcomes of different therapies.

In summary, prostate cancer can affect the patient differently across phases of the disease. There often are no symptoms for many men with early stage, clinically

diagnosed prostate cancer because most prostate cancers arise from the outer peripheral zone of the gland, distant from the urethra (Hernandez & Thompson, 2004). Thus, the suspicion of prostate cancer is usually raised by an elevated serum PSA, abnormal DRE, or both. Depending on the treatment modalities, patients with localized prostate cancer can experience a wide range of symptoms and symptom distress including urinary problems (urinary incontinence and urinary obstruction), sexual dysfunction, bowel problems, and symptom related distress (al-Abany et al., 2002; Bracarda et al., 2005; Clark & Talcott, 2001; Damber & Aus, 2008).

### Stress

Stress can affect an individual's disease and has been studied in different health related areas (Petticrew, Fraser, & Regan, 1999). Hans Selye (1946) first described the concept of stress as a nonspecific response of the body to any demand. He viewed stress as the body's biological response to a perceived emotional or physical threat. In the stress response of Selye's Model, the stress response was characterized by the same chain of events and the same pattern of physiological correlates, regardless of the cause, situational context, or psychological interpretation of a demanding situation. The function of the stress response (the physiological stress response) is to maintain the body's dynamic steady state (Selye, 1946, 1956, 1973; Shelby & McCance, 2001).

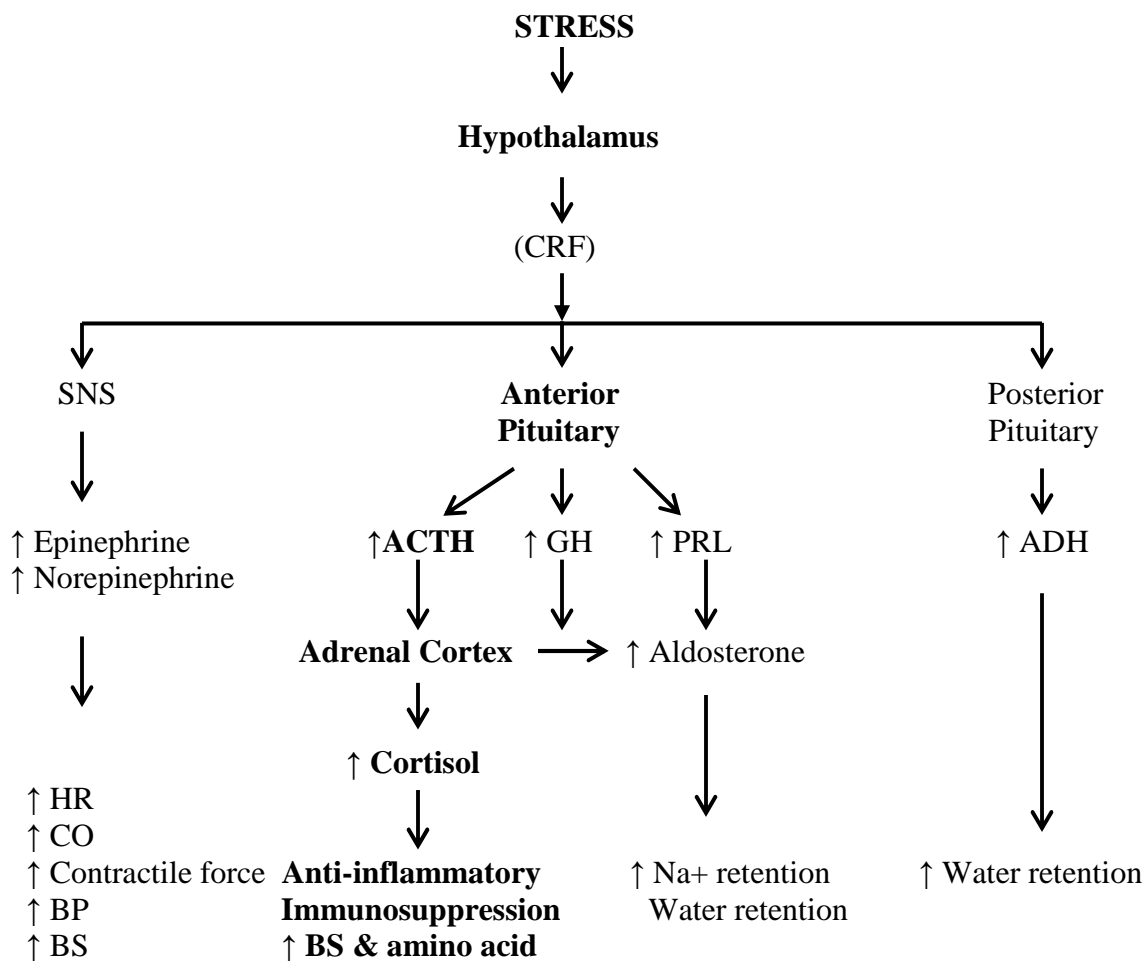
### Physiological Stress Response

Hans Selye (1946) first defined that physiological stress as a chemical or physical disturbance in the cells or tissue fluid produced by a change, either in the external environment or within the body itself, requires a response to counteract the disturbance.

The physiological stress response has a three-fold mechanism consisting of (1) the direct effect of the stressor on the body; (2) internal responses that stimulate tissue defense or help to destroy damaging substances; and (3) internal responses that cause tissue surrender by inhibiting an unnecessary or excessive defense (Selye, 1946, 1973, 1985).

The physiological stress response is initiated when a stressor is present in the body or perceived by the mind. The sympathetic branch of the autonomic nervous system, the endocrine system (pituitary and adrenal glands), and the immune system are all involved in the physiological stress response (Maddock & Pariante, 2001; Segerstrom & Miller, 2004). The pathways of the physiological response to stress are depicted in Figure 4.

Figure 4.

*The Pathway of Physiological Stress Response*

The pathway of physiological stress response

*(Adapted from: Shelby & McCance, 2001)*

(HR = heart rate; CO = cardio output; BP = blood pressure; BS = blood sugar;

CRF = corticotrophin-releasing factor SNS = sympathetic nervous system;

ACTH = Adrenocorticotrophic hormones; GH = growth hormone; PRL= prolactin;

ADH = antidiuretic hormone; Na = sodium)

**(↑ Cortisol is the pathway of interest in this study)**

The physiological stress response is activated by the sympathetic nervous system (SNS) and the endocrine systems. In response to stress, corticotrophin-releasing factor (CRF) is released from the hypothalamus and stimulates release of ACTH from the pituitary gland. ACTH subsequently stimulates release of cortisol from the adrenal cortex. The neuroendocrine response to stress consists of sympathetic stimulation of the adrenal medulla to secrete catecholamines (norepinephrine and epinephrine) and stressor-induced stimulation of the pituitary to secrete adrenocorticotrophic hormones (ACTH), which in turn stimulates the adrenal cortex to secrete steroid hormones, particularly cortisol (Maddock & Pariante, 2001; Shelby & McCance, 2001).

During the physiological stress response, the sympathetic nervous system (SNS) is aroused and causes the medulla of the adrenal gland to release catecholamines (epinephrine, norepinephrine, and dopamine) into the bloodstream. Simultaneously, hypothalamic corticotrophin-releasing hormone (CRH) stimulates the pituitary gland to release a variety of hormones, including antidiuretic hormone (ADH), from the posterior pituitary gland; and prolactin (PRL), growth hormone (GH), and adrenocorticotrophic hormones (ACTH) from the anterior pituitary gland. ACTH stimulate the cortex of the adrenal gland to release cortisol (Herbert & Cohen, 1993; Shelby & McCance, 2001). See Figure 4.

During the physiological response to the stress, the catecholamines (epinephrine, norepinephrine, and dopamine) are release to prepare the body to act, and cortisol mobilizes glucose and other substances such as amino acids needed for metabolism. Epinephrine and norepinephrine exert their chief effects on the cardiovascular system.



Epinephrine increases cardiac output and increases blood flow to the heart, brain, and skeletal muscles by dilating vessels that supply these organs. Epinephrine also dilates the airways, thereby increasing delivery of oxygen to the blood stream. Simultaneously, norepinephrine constricts blood vessels of the viscera and skin; this has the effect of shifting blood flow to the vessels dilated by epinephrine. Norepinephrine also increases mental alertness (Chrousos, 1992; Herbert & Cohen, 1993; Maddock & Pariente, 2001; Shelby & McCance, 2001).

In the pathway of the physiological stress response, the adrenal cortex is activated by ACTH released from the anterior pituitary to increase secretion of glucocorticoid (steroid) hormones, primary cortisol. The chief effects of cortisol are on metabolic processes. Cortisol mobilizes glucose, amino acids, lipids, and fatty acids and delivers them to the bloodstream. Cortisol also inhibits glucose uptake and metabolism in many cells, and suppresses immune and inflammatory function (Chrousos & Gold, 1992; Shelby & McCance, 2001). Selye (1956) proposed that the elevation of cortisol is a feature of the physiological stress response (Selye, 1956). Cortisol has been described as a “stress ” hormone and studies have shown a relationship between cortisol, stress, psychological distress and adjustment in cancer patients (Sephton, Sapolsky, Kraemer, & Spiegel, 2000; Spiegel & Sephton, 2001; Vedhara, Tuinstra, Miles, Sanderman, & Ranchor, 2006).

Other hormones are released and affected during the physiological response to stress. For example, GH and PRL are synthesized and released from the anterior pituitary gland. The function of GH is involved in tissue repair and participates in the growth and

function of the immune system. PRL is for lactation and breast development. The adrenal cortex also increases the secretion of aldosterone during stress by ACTH. Aldosterone increases sodium and water retention. Additionally, the release of ADH from the posterior pituitary during the physiological stress response stimulates water retention and increases fluid volume in the body (Shelby & McCance, 2001; Spiegel & Sephton, 2001). The main function and the optimal goal of the physiological stress response are to maintain body's homeostasis.

In summary, the HPA axis and the SNS are two principal biological components of the physiological response to stress. CRH activates the HPA axis and the SNS leads to an increase in glucose, heart rate, and blood pressure. Regulation of the immune response occurs alongside behavioral changes including enhanced arousal and vigilance, and suppression of feeding and reproductive behaviour (Maddock & Pariente, 2001). The nervous, endocrine, and immune systems communicate through signaling molecules and their receptors, which in turn regulate the behavior of cells in each system during a stress challenge. The goal of the physiological stress response is to maintain the body's dynamic steady state.

### Psychological Stress Response

The psychological stress response may include perception, appraisal, and coping with situations an individual encounters. A single consistent definition of the psychological stress response was not found. Lazarus and Folkman (1984) proposed the transactional model of stress and coping (Lazarus & Folkman, 1984). Stress, appraisal, and coping are three main components in the transactional model. In this model, stress is

defined as a relationship between the individual and the environment that is appraised by the individual as taxing or exceeding his or her resources and endangering his or her well-being. In the transactional model of stress and coping, Lazarus and Folkman view stress as a transactional process and focus on the appraisal process and coping (Lazarus & Folkman, 1984; Lazarus, 1966; Lazarus & DeLongis, 1983).

Other researchers defined stress as life events that create change and require adaptation based on the perspective of the psychological stress response (Kanner, Coyne, Schaefer, & Lazarus, 1981; Lazarus & DeLongis, 1983). In his stress theory, Selye also mentioned the perception of stress but did not propose any measurement related to psychological stress. Selye (1956) viewed stress as the body's biological response to a perceived emotional or physical threat (Selye, 1956).

Perceived stress was first proposed by Cohen and his colleagues in 1983; they defined perceived stress as the degree to which the individual appraises events as unpredictable, uncontrollable, and overloading (Cohen, Kamarck, & Mermelstein, 1983; Cohen & Williamson, 1988). Perceived stress is based on the relationship between the person and the environment. Cohen (1983) developed a global and event-specific measure of perceived stress which is based on how the person perceives or evaluates a situation as stressful or not stressful.

In summary, the psychological stress response may include perception, appraisal, and coping with situations an individual encounters. Based on the review of literature, there is no unifying definition of the psychological stress response. Additionally, there is inconsistency between the definitions (theoretical and operational) and the measurement

of the psychological stress response. In this study, psychological stress response was represented by perceived stress. Perceived stress was defined as how patients treated with localized prostate cancer perceive or evaluate the situations as stressful or not stressful, specifically to the treatment modalities, symptoms, and symptom distress 1-3 months after their first treatment.

#### Relevant Research on Salivary Cortisol, Perceived Stress and Localized Prostate Cancer

Studies have shown correlational evidence that suggests that the physiologic stress responses are associated with poor adjustment to cancer and may, indeed, speed disease progression (Spiegel & Sephton, 2001). There is growing evidence that the functioning of the HPA axis has profound effects on the body's ability to fight disease progression. Activation of the HPA axis is an adaptative response to acute stress, but over time in response to cumulative stress the system's ability to respond only when needed can be degraded. Dysregulation of stress hormones such as cortisol has been found to be associated with worse disease prognosis. Persistently elevated or relatively invariant levels of cortisol may stimulate tumor proliferation via differential gluconeogenesis in normal and tumor tissue or activation of hormone receptors in tumor, or immunosuppression.

Stress has been studied in different health related conditions, but the specific stress-induced mechanisms are not clearly defined. Recent research focused on the regulatory interactions among the immune, nervous, and endocrine systems, which may represent mechanistic pathways for stress-associated immune-mediated diseases, including infection, some forms of cancer, allergy, and autoimmunity (Cohen & Rabin,

1998; Maddock & Pariante, 2001; Spiegel & Sephton, 2001). Mechanisms have been proposed whereby the neuroendocrine correlates of stress may promote neoplastic growth (Lacey et al., 2000; Spiegel & Sephton, 2001).

Stress hormones may suppress immune resistance to the tumor, or act via differential effects on gluconeogenesis in healthy versus tumor cells. Tumor cells may become resistant to the catabolic action of cortisol which inhibits the uptake of glucose in numerous cell types. In such cases, metabolic resources would be preferentially shunted to the tumor and away from normal cells by cortisol. Several studies have found an association between stress-related elevation of glucocorticoids and more rapid tumor growth in animals (Lacey et al., 2000). Another hypothesis suggests that hormones of the HPA axis may actually promote the expression of breast cancer oncogenes (Spiegel & Sephton, 2001).

In addition, there is evidence that stress-related increases in SNS and HPA activity suppress immune functions which can result in increase tumor growth. Elevation of glucocorticoids is associated with clinically significant immunosuppression, and enhanced secretion of norepinephrine during stress has also been associated with suppression of lymphocyte function (Spiegel & Sephton, 2001). There is evidence that both psychoneuroimmune and endocrine physiologic pathways can affect the course of cancer progression. Furthermore, the immune system is a salient transducer and influences the disease course. These pathways likely interact with one another as well.

Cortisol is potently immunosuppressive, and elevated levels of it and/or lack of physiologic release during normally low diurnal periods may compromise components of

immune function that can affect cancer progression (Herbert & Cohen, 1993). There is evidence that psychological stress might alter immune function through a number of mechanisms (Cohen & Rabin, 1998). These mechanisms include direct innervations of lymphatic tissue by the central nervous system and stress-elicited release of hormones from the brain that bind to and alter the functions of immunologically active cells. For example, direct suppressive effects of corticotrophin-releasing hormone (CRH) have been reported on two immune cell types expressing CRF receptors: the monocyte-macrophage and T helper (CD<sub>4</sub>) lymphocyte (Lacey et al., 2000; Spiegel & Sephton, 2001).

Release of endogenous opiates occurs during stress, and these peptides have been shown to have concentration-dependent, enhancing, and suppressive effects on various immune cells. Indirect effects of the central nervous system on immune function involve the HPA axis. It was noted that the adrenal gland enlarged with simultaneous involution of the thymus and lymph nodes. Increased levels of circulating glucocorticoids are thought to be an important mechanism, both in the stress-related alternations in immune structures and in suppression of immune response (Lacey et al., 2000; Segerstrom & Miller, 2004; Spiegel & Sephton, 2001).

Behavioral changes are involved in the stress mechanisms where people's efforts to manage the demands of a stressful experience sometimes lead them to engage in behavioral changes (Segerstrom & Miller, 2004). In stressful situations, people may adapt behavioral changes that can have negative effects on their health. These behavioral changes include increase in cigarette smoking, increase in drinking alcohol, loss of sleep, reduction in exercise, degradation of the diet, and decrease in adherence to medical

regimens or symptom management. Thus, behavior represents a potentially important pathway linking stress with the immune system and health performance (Cohen & Rabin, 1998; Maddock & Pariante, 2001; Segerstrom & Miller, 2004). Studies have shown that patients with breast cancer and prostate cancer have abnormal cortisol secretion patterns (abnormal cortisol circadian rhythm), and have demonstrated that stress reduction intervention (mindfulness-based stress program) is associated with enhanced quality of life and decreased stress response and symptoms (Carlson et al., 2004; Mormont & Levi, 1997; Sephton et al., 2000).

Smyth et al. (1997) reported that salivary cortisol increased with daily stressors and anticipated stress (Smyth et al., 1997). Several investigators found that increased levels of perceived stress were associated with increased concentrations of salivary cortisol (Van Eck & Nicolson, 1994; Vedhara, Fox, & Wang, 1999). Pruessner et al. (1999) demonstrated that perceived stress correlated with increased cortisol levels during the first hour after awakening after dexamethasone pretreatment (Pruessner et al., 1999). However, Lasikiewicz et al. (2008) found neither perceived stress nor daily hassles were significant predictors of cortisol profile (Lasikiewicz, Hendrickx, Talbot, & Dye, 2008).

In summary, stress leads to the activation of the HPA axis. Stressful experiences may influence neuroendocrine, immune functioning as well as physical and psychological well-being. High stress can affect an individual's health performance through the interaction among immune system, endocrine system, nerve system, and behavioral regulations (Maddock & Pariante, 2001; Spiegel & Sephton, 2001). Little research has focused on physiological and psychological stress responses among men

treated with localized prostate cancer. It is important to determine the level of stress responses specifically to measure the physiological stress response by using a biological marker (saliva cortisol) and to explore the relationship between saliva cortisol and perceived stress among man with localized prostate cancer following radical prostatectomy or radiation therapy.

### Symptoms

One definition of the term symptom is a subjective phenomenon regarded by an individual as an indication or characteristic of a condition departing from normal function, sensation, or appearance (Morris, 2002). According to the Oxford English Dictionary, a symptom is defined as a bodily or mental phenomenon, circumstance, or change of condition arising from and accompanying a disease or affection, and constituting an indication or evidence of it; and a characteristic sign of some particular disease (University, 2005). The National Cancer Institute (2008) defines a symptom as an indication that a person has a condition or disease (National Cancer Institute, 2008).

Researchers in nursing have defined symptoms as distinctive features of diseases that are used to diagnose a patient's condition and often include signs or objective clinical manifestations (Armstrong, 2003; Goodell & Nail, 2005; Portenoy et al., 1994; Rhodes & Watson, 1987; Watson, Rhodes, & Germino, 1987). A symptom is an experience that is perceived and verified only by the individual experiencing the phenomenon; therefore, the symptom is subjective and experiential (Fu et al., 2004; McDaniel & Rhodes, 1995; Rhodes & McDaniel, 1999). Symptoms can be viewed also as inevitable side-effects of therapy, particularly by a physician (Armstrong, 2003).



### Symptom Distress

The concepts of distress and symptom distress are often used interchangeably. Distress can be defined as a commonly used derivative of the word stress (Rhodes, McDaniel, Homan, Johnson, & Madsen, 2000; Rhodes & Watson, 1987). When Selye (1956) first defined the term ‘stress’, he proposed subdefinitions of stress, ‘eustress’ and ‘distress’. Selye (1956) proposed that distress encompassed the more severe, protracted, and uncontrollable situations (both psychologically and physically) that led to disease states (Selye, 1956). Distress also can be defined as physical or mental suffering or anguish (Morris, 2002); the amount of upset sensations cause (Leventhal, Brown, Shacham, & Engquist, 1979); or as suffering and upset (Nightengale, 1946).

In the Theory of Unpleasant Symptoms, Lenz et al. (1995) defined distress as one of four dimensions of a symptom and that it reflects the degree to which a person is bothered by a symptom (Lenz et al., 1997; Lenz et al., 1995). The National Comprehensive Cancer Network (2004) defined distress as a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment (Network, 2004). Distress is another component of symptoms that can be measured with self-report tools (Rhodes & Watson, 1987).

Symptom distress can be defined as “the degree of discomfort from a specific symptom the patients perceived to experience” (McCorkle & Young, 1978); or “physical or mental anguish or suffering that results from the experience of symptom occurrence” (Watson et al., 1987). Researchers in nursing defined symptom distress as the degree of

physical or mental suffering, discomfort, or bother reported by individuals in relation to their perceptions of the symptom (Lenz et al., 1997; McCorkle & Benoliel, 1983; Portenoy et al., 1994; Rhodes et al., 2000; Rhodes & Watson, 1987).

Symptom distress may include thoughts related to the symptom, the degree of attention given to the symptom, and the mood or mental outlook of the person, and the situational context of the symptom occurrence (Rhodes et al., 2000; Rhodes & Watson, 1987). Symptom distress is an aspect of the symptom experience that includes the human response to symptom occurrence, i.e. awareness of the distress and recognition of the degree of upset, strain, and mental anguish (McCorkle & Young, 1978; Rhodes et al., 2000).

Bother is another term closely associated with symptom distress (Goodell & Nail, 2005). Previous studies evaluated symptom distress by asking subject “how much a symptom bothered them” or “how much a symptom bothers or distresses them” (Johnson, 1973; Portenoy et al., 1994). In Merriam-Webster, Incorporated (2005), bother is synonymous with irk and pester, as to annoy, especially by extremely provocation (Merriam-Webster, 2005). Distress is synonymous with being upset, and is defined as a state of being in great trouble. Other related concepts include symptom occurrence, symptom experience, symptom awareness, and symptom perception. These related terms are different concepts from symptom distress. Symptom distress and symptom occurrence are critical components of symptom experience. Symptom occurrence includes frequency, duration, and intensity (severity) of the symptom, whereas symptom

distress is the degree of discomfort a patient reports in response to a specific symptom he experienced (Armstrong, 2003; Cooley, Short, & Moriarty, 2002).

Symptom distress provides the most useful information about quality of life if a single symptom assessment measure is preferred; a frequency measure adds significant information (Armstrong, 2003; Portenoy et al., 1994). Therefore, many studies have used symptom distress as one of the indicators of health-related quality of life. However, to capture a measurement of symptom distress, the researcher needs to recognize the exact theoretical and operational definitions of symptom distress. The critical attributes of symptom distress include:

1. Physical or mental suffering, anguish, upset, discomfort, or bother.
2. Results from a specific symptom occurrence and/or the perception of feeling states.
3. Experienced or reported by individuals in relation to their perceptions of the symptom.
4. The need to alter (restrain or produce) actions in response to a subjective indication of disease (Goodell & Nail, 2005; McClement et al., 1997; McCorkle & Young, 1978; Rhodes et al., 2000; Rhodes & Watson, 1987).

#### Relevant Research on Symptoms, Symptom Distress and Localized Prostate Cancer

Many studies of patients treated with localized prostate cancer focused on health-related quality of life, and the researchers defined symptoms and symptom distress as one of the outcome variables or indicators of health-related quality of life (al-Abany et al.,

2002; Galbraith, Arechiga, Ramirez, & Pedro, 2005; Korfage et al., 2005; Seo et al., 2004; Visser et al., 2003; Wright et al., 2008).

Symptoms associated with localized prostate cancer include bladder outlet obstructive symptoms (dysuria, dribbling, decreased force of the urinary stream, or incomplete bladder emptying), irritating voiding symptoms (urinary frequency or nocturia), hematospermia, decreased ejaculatory volume, or impotence (Damber & Aus, 2008; Hernandez & Thompson, 2004; Rose, Shrader-Bogen, Korlath, Priem, & Larson, 1996; Zeller, 2008). Several studies reported that men treated with localized prostate cancer experienced moderate to severe symptoms and symptom related distress in urinary, bowel, and sexual functioning after different treatment modalities (Clark, Bokhour et al., 2003; Clark & Talcott, 2001; Lepore, Helgeson, Eton, & Schulz, 2003; Litwin et al., 2007; Madalinska et al., 2001; Miller et al., 2005; Miller et al., 2007; Penson, 2007; Penson & Litwin, 2003).

Men with localized prostate cancer undergoing radical prostatectomy reported more urinary problems (urinary leakage, incontinence, dribbling, and nocturia) and more sexual dysfunction (erectile dysfunction, dissatisfaction) than men receiving radiation therapy (Lilleby, Fossa, Waehre, & Olsen, 1999; Stanford et al., 2000; Wright et al., 2008; Yarbro & Ferrans, 1998). Postoperative patients felt greater negativity regarding physical appearance, state of health, and sexuality (Perez et al., 1997; Perez, Skinner, & Meyerowitz, 2002; Wright et al., 2008). One comparison study reported that men treated with radical prostatectomy had a higher rate of physiological impotence (86%) than men treated with external beam radiation (57%) (Litwin et al., 2007). Yet, Perez, Skinner and

Meyerowitz (2002) found that men who received radical prostatectomy 2-year later reported low levels of emotional distress and satisfaction with the treatment (Perez et al., 2002). As the disease progresses, blood may be present in the semen along with decreased ejaculatory volume and impotence (Steineck et al., 2002; Yarbrow & Ferrans, 1998).

Previous studies found that patients treated with prostatectomy usually had higher distress associated with urinary and sexual functioning, while those treated with radiation therapy had higher bowel problem distress (Bradley, Bissonette, & Theodorescu, 2004; Buron et al., 2007; Clark, Inui et al., 2003; Clark & Talcott, 2001; Henningsohn, Steven, Kallestrup, & Steineck, 2002; Korfage et al., 2005; Litwin et al., 2007; Schapira, Lawrence, Katz, McAuliffe, & Nattinger, 2001). Damber and Aus (2008) documented that 20-100 % of patients with localized prostate cancer treated by prostatectomy developed erectile dysfunction and 0-70 % experienced moderate to severe urinary incontinence (Damber & Aus, 2008).

Previous studies found that symptoms and symptom distress were correlated with each other (Clark & Talcott, 2001; Talcott, Clark, Manola, & Mitchell, 2006). Clark and Talcott (2001) reported significant correlations between pairs of function (symptoms) and distress indexes ( $r = 0.63-0.84$ ), and between the level of function (symptoms) and patient distress scores (Clark & Talcott, 2001; Talcott et al., 2006). Litwin and colleagues also found that health related quality of life among men treated for early stage prostate cancer was correlated with measures of function and bother in urinary, sexual, and bowel (Litwin et al., 2007; Litwin et al., 1998).

In summary, men with prostate cancer treated with prostatectomy or radiation therapy can have different symptoms and symptom distress. Some studies have not used theoretical or operational definitions of symptoms and symptom distress to measure these concepts (Clark & Talcott, 2001; Henderson, Laing, & Langley, 2004; Litwin et al., 1998; Rosenfeld et al., 2004; Schapira et al., 2001; Steineck et al., 2002; Talcott et al., 2003; Wei, Dunn, Litwin, Sandler, & Sanda, 2000; Wei, Dunn, Marcovich, Montie, & Sanda, 2000). Therefore, it is important to use valid measures of symptoms and symptom distress based on operational definition and to investigate differences in symptoms and symptom distress among men with localized prostate cancer based on type of treatment.

#### Symptom Self-Management

A consistent definition of symptom self-management was not found in the literature. Symptom self-management, symptom management, and self-management are often used interchangeably (Fu et al., 2004). For this study the concept of symptom self-management was developed by combining symptom management and self-management.

As discussed previously, symptom is defined as a bodily or mental phenomenon, circumstance, or change of condition arising from and accompanying a disease or affection. A symptom can also indicate the presence of a particular disease (University, 2005). Nurse researchers have defined symptom as: 1) a subjective experience reflecting changes in biopsychosocial functioning, sensations, or cognition of an individual; or 2) an experience that is perceived and verified only by the individual experiencing the phenomenon. Therefore, a symptom is subjective and experiential or a perceived

indicator of a change in normal functioning as experienced by patients (M. Dodd et al., 2001; Fu et al., 2004; Lenz et al., 1997).

Management is defined as “the application of skill or care in the manipulation, use, treatment, or control (of things or persons); or in the conduct of something” (University, 2005). Management is also defined as “the act or art of managing; the conducting or supervising of something; judicious use of means to accomplish an end; the collective body of whom of those who manage or direct an enterprise (Merriam-Webster, 2005).

Symptom management has been conceptualized as self-monitoring, self-care, self-regulation, self-management, or self-treatment (M. Dodd et al., 2001; Fu et al., 2004; Lenz et al., 1997; Rhodes et al., 2000; Richardson & Ream, 1997). The National Cancer Institute (2008) defines symptom management as care that is given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of symptom management is to prevent or treat as early as possible the symptoms of the disease, side effects caused by treating the disease, and psychological, social, and spiritual problems related to the disease or its treatment (National Cancer Institute, 2008).

Fu et al (2004) systematically analyzed the concept of symptom management in patients with cancer, and defined symptom management as “a dynamic and multidimensional process in which patients, intentionally and purposefully act on and interact with their symptom perception (or previous perception) to initiate activities or direct others to perform activities to relieve or decrease distress from and prevent the

occurrence of a symptom” (Fu et al., 2004). The author also summarized the essential attributes of symptom self-management. These attributes include the following:

1. Subjective: The person’s perception (or previous perception) of the symptom experience and the degree of symptom distress to consciously realize and evaluate the need to manage the symptom (s). The person will make decisions and carry out activities to alleviate, control, or prevent the symptom (s).
2. Experiential: Symptom management only emerges in an experience in which individuals interact with the perception of the symptom to initiate activities to relieve or decrease distress from the symptom experience.
3. Intentional: Individuals purposefully undertake activities to manage the symptom they experienced. Intentional activities involve perception, cognition, affection, and other conscious acts.
4. Multidimensional: Symptom management includes physical, perceptual, psychological, cognitive, and sociocultural dimensions. Symptom management is multidimensional.
5. Dynamic process: Symptom management is a dynamic process including phases of evaluation, decision making, actual management, and outcome (Fu et al., 2004).

Symptom occurrence and symptom distress influence symptom management (Fu et al., 2004). Studies have shown that multiple factors affect symptom distress and symptom occurrence; for example, Lenz et al. (1997) proposed three categories of variables that are antecedents to unpleasant symptoms. The categories are physiologic



factors, psychological factors, and situational factors (Lenz et al., 1997; Lenz et al., 1995). Rhodes and Watson (1987) concluded that the perceptions, evaluations, and response to illness influence life routines, chronicity, attainment of proper care, and participation in self-care practice (Rhodes & Watson, 1987).

In addition, factors that affect an individual's perception of symptom distress include age, gender, culture, family role, education, health knowledge, type of treatment, values, beliefs, and past experience (Juarez, Ferrell, & Borneman, 1999; McClement et al., 1997; Rhodes, McDaniel, & Johnson, 1995). Tishelman, Taube, and Sachs (1991) reported that gender, age, marital status, sense of coherence (an enduring and dynamic feeling of confidence), and the type of treatment were found to be significantly related to patients' degree of symptom distress (Tishelman, Taube, & Sachs, 1991). Therefore, the influential factors of symptom occurrence and symptom distress are the antecedent factors of symptom management.

Symptom management has positive and negative outcomes. Positive outcomes include relief of the symptom, a decreased severity of symptom distress, prevention of symptom occurrence, and improved quality of life. Negative outcomes include recurrence of the symptom, sustained or increased degree of symptom distress, and stable or decreased quality of life (Fu et al., 2004). Some researcher proposed that symptoms or symptom distress is considered one of the outcome indicators for symptom management (Dimeo, Rumberger, & Keul, 1998; Dodd, Miaskowski, & Paul, 2001; Fu et al., 2004; MacVicar, Winningham, & Nickel, 1989; Porock, Kristjanson, Tinnelly, Duke, & Blight, 2000; Rhodes et al., 2000). Studies have shown that effective symptom management can

decrease symptom distress and improve quality of life and survival among patients with cancer (Fu et al., 2004). Symptom management is related to quality of life, treatment tolerance, and survival in patients with cancer and other illnesses (Goodell & Nail, 2005; McCorkle & Benoliel, 1983; Portenoy et al., 1994).

In summary, the antecedents of symptom self-management can be categorized as physiologic factors, psychological factors, and situational factors. There are also personal characteristic factors (age, gender, marital status, culture, family role, education, health knowledge, values, beliefs, and past experience), disease related characteristic factors (diagnosis, stage of disease, and type of treatment), and cognitive factors (perceptions, evaluations, and responses to illness) that influence symptom self-management. The outcome indicators or the consequences of symptom management include: symptom status, health related quality of life, performance and survival (M. Dodd et al., 2001; Fu et al., 2004; Lenz et al., 1997; Lenz et al., 1995). Symptom status is a direct outcome of symptom management. Effective management of a symptom should lead to relief of symptoms, improvement in symptom distress, or prevention of symptom occurrence (Fu et al., 2004).

#### Relevant Research on Symptom Self-Management and Localized Prostate Cancer

Very few studies have focused on symptom self-management among men treated with localized prostate cancer. The majority of studies of men with localized prostate cancer are related to quality of life or distressful symptoms following different treatment modalities. Most symptom management or symptom self-management studies have targeted populations with HIV/AIDS, chronic disease, or a mental disorder (i.e.

schizophrenia) (Bunch, 2004; Fuller, Welch, Backer, & Rawl, 2005; Sukati, Makoa, Makoe, Human, & Holzemer, 2005; Tasi, Hsiung, & Holzemer, 2002; Wright, 2003). For example, Chou (2002) conducted a descriptive study to determine self-care strategies and self-care information resources, and significant predictors among patients with HIV/AIDS. The findings showed that there were eight categories of self-care strategies and four sources of self-care information. The self-care strategies included medication, self-comforting, complementary treatments daily thought/activities, changing diet, help seeking, spiritual care, and exercise. The sources of self-care information were self, health care provider, personal network, and community (Chou, 2002).

Chou (2004) further proposed a model of the use of self-care strategies to predict the significant factors for symptom management among individuals (n=359) with HIV/AIDS. The results showed that 1). Self-care strategies include medications, complementary treatments, self-comforting, daily thoughts/ activities, changing diet, help-seeking, exercise, and spiritual care; and 2) the overall model significantly predicted the use of self-care strategies. Race and symptom intensity were significant predictors for self-care strategies for individuals with HIV/AIDS (Chou, 2004; Chou, Holzemer, Portillo, & Slaughter, 2004). Findings from previous studies of symptom management among individuals with HIV/AIDS have demonstrated that the most frequent symptoms were neuropathy, depression, and anxiety, and the most commonly used symptom management strategies include medication, self-comforting, complementary treatments, change in diet, seeking help, exercise, spiritual care, daily thoughts/activities walking,

massage, and aromatherapy. The most useful strategies were medications and walking (Bunch, 2004; Sukati et al., 2005; Tasi et al., 2002).

Most studies of symptom management among patients with cancer focused on interventions and mechanisms for the specific symptom but not on symptom management or symptom self-management. For example, Worcester (1991) presented the guidelines and resources for writing a clear care plan and the issues that need to be addressed in coordination of care related to managing symptoms (constipation, anorexia, nausea, vomiting, dyspnea, and pain) among elderly with cancer. Coordinating symptom management involved planning with the home care agency, among professionals and agencies within the community, and with services. The study did not propose any strategies for symptom self-management (Worcester et al., 1991).

Only a few studies of symptom management among men with localized prostate cancer were found. No study of symptom self-management among men with localized prostate cancer was identified in the literature. Some studies focused on a specific treatment modality for men with localized prostate cancer. For example, a study of hormone ablation treatment for prostate cancer patients described the symptoms of andropause, side effects of hormonal ablation therapy, and the strategies to help patients to manage their symptoms (Thompson, Shanafelt, & Loprinzi, 2003).

A systematic review paper focused on evidence-based practice for the management of sexual dysfunction in adults with cancer, defined the current state of knowledge about intervention for this symptom and identified gaps and barriers in the current state of knowledge. The author concluded that sexual dysfunction had been

addressed extensively in the literature in relation to patients with cancer (prostate cancer was included), but information was needed to ascertain the best assessment strategy and the best intervention, along with appropriate outcome criteria (Shell, 2002).

Palmer, Fogarty, Somerfield and Powel (2003) reported that most men (69 %) with prostate cancer following prostatectomy experienced three types of urinary incontinence including stress incontinence symptoms, urge incontinence symptoms, and mixed incontinence symptoms. Stress incontinence symptoms included lifting, coughing, sneezing, exercising, walking, laughing, and climbing stairs. Urge incontinence symptoms were sense of urgency when sleeping, while in shower or tub, hearing running water, when hands are in water, or when placing key in door lock. The mixed incontinence symptoms included bending, standing up, jogging or running, or during sexual relations (Palmer, Fogarty, Somerfield, & Powel, 2003).

Strategies for urinary incontinence were categorized as behavior, containment, and invasive. The behavioral strategies for urinary incontinence were pelvic muscle exercises, sit to void, voiding schedule, limit fluids, or extra fluids. The containment strategies for urinary incontinence include pads, special undergarments, sanitary napkins, tissue paper, penile clamp, condom catheter, or bed pan. The invasive strategies for urinary incontinence were medication, indwelling catheter, or intermittent catheter (Palmer et al., 2003).

Several studies reported that stool frequency, rectal pain, urgency, and bleeding were the most common complications in patients with prostate cancer following radiation therapy (Anthony, 2003; Kornblau et al., 2000; Miller et al., 1999; Stern & Ippoliti, 2003).

tern and Ippoliti (2003) proposed that the nutritional and dietary guidelines for patients with cancer treatment-induced diarrhea included eating small frequent meals slowly, adequate soluble fiber, protein-rich food; drinking ample liquids that are cool or warm not hot or cold; and replacing electrolytes and minerals (Stern & Ippoliti, 2003). Other strategies to alleviate stool frequency, chronic enteritis, or proctitis after high radiation doses included nutritional management (dietary and nutritional guidelines), pharmacologic management (intestinal transit inhibitors and antisecretory agents, or opioids for pain), and surgery (typically required to improve the symptoms of small bowel damage, e.g. severe proctitis) (Anthony, 2003; Kornblau et al., 2000; Miller et al., 1999; Stern & Ippoliti, 2003).

A previous study conducted by Neese et al. (2001) involved a phone survey of men's and women's perspectives on finding help for sexual problems after prostate cancer treatment. Investigators identified 12 strategies for solving sexual problems. The most frequent strategies patients used included: 1. saw an urologist who specialized in sexual problems, 2. asked a prostate cancer specialist for help, 3. read a book or article about sexual problems, 4. asked spouse/partner for advice, and 5. asked a nurse or social worker for help (Neese, Schover, Klein, Zippe, & Kupelian, 2003). These investigators also found that lack of desire for sex was a barrier for men and their partners to seek help for a sexual problem.

In summary, there is limited research on symptom self-management among men with localized prostate cancer. Only a few studies reported strategies for symptom management in men with prostate cancer receiving radical prostatectomy, but these did

not included a measure of perceived effectiveness of symptom management strategies. In order to provide more effective and comprehensive strategies of symptom self-management and to enhance health related quality of life, it is important to identify the effective symptom self-management strategies among patients treated with localized prostate cancer.

## CHAPTER III

### METHODOLOGY

#### Introduction

The research design, sample, setting, data collection procedures, study measures, and data analysis plan are described below. Procedures for protection of human subjects and the methods for salivary cortisol are also summarized.

#### Research Design

This study used a descriptive, correlational, and cross-sectional design to examine the relationships among stress, symptoms, symptom distress, and symptom self-management in men with localized prostate cancer 1-3 months following prostatectomy or radiation therapy. Stress included physiological and psychological stress responses. Symptoms and symptom distress primarily focused on urinary problems, bowel problems, and sexual dysfunction. Symptom self-management consisted of symptom self-management strategies and the perceived effectiveness of these strategies.

#### Sample and Setting

Patients with localized prostate cancer receiving radical prostatectomy or radiation therapy were the targeted sample. Convenience and purposive sampling were used to recruit subjects. Nonprobability sampling (convenience and purposive sampling) decreases the generalizability of study finding because the sample may not be representative of the population of interest. Care was taken to seek a representative sample from the current population of men treated for localized prostate cancer from two large medical centers in the southwestern United States. Men who met the following



inclusion criteria were approached and asked about their interest in participating in this study.

The inclusion criteria included:

- (1) A diagnosis of clinically localized prostate cancer treated with radical prostatectomy or radiation therapy;
- (2) 1-3 months after receiving their first treatment;
- (3) Able to understand and communicate in English.

The exclusion criteria included:

- (1) Factors known to influence cortisol, including night-shift work and use of medications known to affect cortisol levels such as prednisolone or dexamethasone.

### Setting

Research participants were recruited from (1) the Department of Urology, Radiology Oncology in the Arizona Cancer Center, University Medical Center and at the Southern Arizona Veterans Affairs Health Care System, (2) community based urology clinics, and (3) Prostate Cancer Support Groups in Tucson Arizona.

### Sample Size

A power analysis was performed to determine how many subjects should be included in this study. Cohen's formula was used to calculate adequate sample size, effect size, and power. Cohen (2005) defined a small effect size as an  $R^2$  of 0.02, a moderate effect as an  $R^2$  of 0.13, and a large effect size as an  $R^2$  of 0.30 (Cohen, 2005; Munro, 2005).

The formula is:

$$N = \frac{L(1 - R^2)}{R^2} + u + 1$$

Where  $N$  = total sample size

$L$  = effect size index

$u$  = number of independent variables

In this study, a power of 0.80, an alpha of 0.05, and a moderate effect size of 0.13 were selected. There were three independent variables (stress, symptoms and symptom distress), the value of  $L$  (*effect size index*) was 10.90; therefore, the sample size was 77 (Cohen, 2005; Munro, 2005). In addition, Kline (1998) recommends 10 times as many cases as parameters (Kline, 1998). There were five parameters (salivary cortisol, perceived stress, symptoms, symptom distress, and symptom self-management) in the model, so the adequate sample size in this study was 50 according to Kline's rule. Therefore, the estimated sample size of this study was between 50 and 77 according to Cohen and Kline's formula (Cohen, 2005; Kline, 1998).

#### Protection of Human Subject

Approval for the study was obtained from the Human Subjects Committee of the University of Arizona (Appendix A). Approval for the study was also obtained from the Institutional Review Board of the Southern Arizona Veterans Affairs Health Care System Research and Development Review Committee (Appendix A).

The investigator reviewed the informed consent form with each participant and asked questions to be certain that he understood the information in the consent form. The investigator thoroughly explained the study to the participants and allowed them to

voluntarily choose to participate or not. Participants were informed of the risks and benefits of the study and advised that they were free to withdraw from the study at any time. For salivary cortisol, there was a 4-5 hour period for sample collection and each participant was given a schedule with colorful reminders to minimize the potential burden for collecting the saliva sample in a required period. To ensure subject confidentiality, each participant was assigned a code number and identifiable information was not reported. Prior to participation in this study, an informed consent was signed and obtained from each participant. Informed consent is attached in Appendix B.

#### Study Variables and Measures

The main variables of this study were stress (physiological stress response and psychological stress response), symptoms, symptom distress, and symptom self-management (symptom self-management strategies and perceived effectiveness). The main variables and measures are described below according to study aims.

**Aim One:** To examine physiological and psychological stress responses in men with localized prostate cancer following radical prostatectomy or radiation therapy.

#### Measurement of Stress: Physiological Stress Response

The physiological stress response was measured by salivary cortisol including the levels and circadian patterns of salivary cortisol. In recent years, cortisol has been described as a “stress” hormone and studies have shown a relationship between cortisol, stress, psychological distress and adjustment in cancer patients (Carlson et al., 2004; Sephton et al., 2000; Stone, 2001). Cortisol is the end product of HPA axis activation. During the stress response, cortisol secretion by the adrenal cortex is initiated by the

release of corticotrophin-releasing factor from the hypothalamus which acts on the pituitary to secrete adrenocorticotrophic hormone which regulates the release of cortisol (Kirschbaum & Hellhammer, 1994; Kirschbaum, Strasburger, Jammers, & Hellhammer, 1989). Hans Selye's stress model, was the first to describe stress as the body's biological response to a perceived emotional or physical threat and later noted that a feature of this response was an elevation of cortisol (Herbert & Cohen, 1993; Selye, 1956).

Previous studies have shown that cortisol is a reliable physiological stress measure and can be used as an indicator of physiological stress and psychological stress (Kirschbaum & Hellhammer, 1994; Kirschbaum, Strasburger, Jammer, & Hellhammer, 1989; Lac, 2001; Lac, Lac, & Robert, 1993; Vining, McGinley, Maksvytis, & Ho, 1983). According to the literature, the average salivary level varies from  $15 \text{ nmol} \cdot \text{l}^{-1}$  at awaking to  $3 \text{ nmol} \cdot \text{l}^{-1}$  at night time. Salivary cortisol has been used in clinical and research biology and validated by different studies (Lac, 2001). The correlations between salivary cortisol and serum cortisol were shown to be very high (from 0.6 to 0.9) in previous studies (Kirschbaum & Hellhammer, 1994; C. Kirschbaum et al., 1989; Lac, 2001; Lac et al., 1993; Vining & McGinley, 1987; Vining et al., 1983).

Saliva assays have been successfully used since the beginning of the 1980s. Salivary cortisol is also used clinically for the ACTH stimulation test, dexamethasone suppression test, for follow-up of Cushing syndrome, psychological disorders, and the analysis of any situation of stress (Lac, 2001; Stahl & Dorner, 1982). Salivary assays have the advantage of being less invasive compared to serum. Salivary samples are easy to collect in a non medical environment (Lac, 2001; Levine, Zagoory-Sharon, Feldman,

Lewis, & Weller, 2007). Therefore, salivary cortisol was used to indicate the physiological stress response including the levels and circadian rhythm of cortisol in this study.

*Measures: Salivary Cortisol*

Salivary cortisol was measured by an enzyme-linked immunoabsorbent technique (ELISA). The performance of any immunoassay is directly dependent on the quality of the antigen used as a target or labeled detector and the antibody used as to capture or detect (Shirtcliff, Granger, Schwartz, & Curran, 2001). Total salivary cortisol was assessed by using the High-Sensitivity HS Salivary Cortisol Enzyme Immunoassay (Salimetrics, Inc., State College, PA). Sensitivity of the assay was .007ug/dL. Intra-assay coefficients of variation were between 3.9 % and 7.1 % while inter-assay coefficients were between 6.7 % and 6.9 % (Salimetrics, 2007; Stewart & Seeman, 2000). In order to characterize the circadian rhythm, samples were collected at 4 time points: on awakening, noon (11 AM -12 PM), afternoon (4 - 5 PM) and evening (9 - 10 PM) over 2 days.

The Salivette collection device was used to obtain saliva samples. The investigator instructed the participants to follow the protocol for collecting saliva samples. Participants placed the cotton swab from the Salivette into their mouth under the tongue for at least 2 minutes while it became saturated with saliva, then placed the cotton swab back into the collection device (special plastic tube). Samples were stored in a freezer at each participant's house right after the sample was collected. Saliva samples are stable at room temperature for up to 3 weeks (Levine et al., 2007). Saliva samples were collected from each participant's house by the investigator within 7 days after all

saliva samples and measures were completed. Table 1 summarizes the procedure for collecting saliva samples. The protocol for collecting salivary cortisol is attached in Appendix C.

Table 1.

*Procedure for Collecting Saliva Samples*

<p><b>Time:</b></p> <p>Collect sample at the time of 1) awakening (before getting out of bed), 2) 11~12 pm (around noon), 3) 4~5 pm (afternoon), and 4) 9~10 pm (evening) for 2 day sequentially.</p>
<p><b>Note:</b></p> <ol style="list-style-type: none"> <li>1. Do not brush teeth or consume any alcohol 30 minutes before collecting the saliva.</li> <li>2. Do not eat meals, foods, or snacks 30 minutes before collecting the saliva.</li> <li>3. Rinse mouth with water 10 minutes before collecting the saliva.</li> </ol>
<p><b>Procedure:</b></p> <ol style="list-style-type: none"> <li>1. Before getting out of bed, please collect the first sample when you wake up (open your eyes) in the morning.</li> <li>2. Place one cotton stick (swab) in mouth, under tongue, at least for 1-2 minutes.</li> <li>3. Put the saturated cotton stick (swab) in the plastic tube.</li> <li>4. Place another cotton stick (swab) in mouth, under tongue, for 1-2 minutes.</li> <li>5. Put the saturated cotton stick (swab) in the special plastic tube (<b>2 saturated cotton sticks should be placed in a color coded plastic tube for each collection</b>).</li> <li>6. Mark the plastic tube with the time and the date (or put the color sticker on the tube that indicates the time and the date for collecting saliva).</li> </ol>
<p><b>Note:</b></p> <ol style="list-style-type: none"> <li>1. Inspect for visible blood contamination, if contaminated; please make a note of it.</li> <li>2. Make a daily log to explain if there is anything unusual happening during the day with collecting sample (e.g. unexpected visitor or phone call...)</li> </ol>
<p><b>Store:</b></p> <ol style="list-style-type: none"> <li>1. Store the saliva samples in the freezer at your house.</li> <li>2. I will come to your house to pick up the sample in 7 days after you complete all sample collections.</li> </ol>
<p><b><i>I deeply appreciate with your co-ordination and help.</i></b>  <b><i>THANK YOU VERY MUCH!!</i></b></p>

### Measurement of Stress: Psychological Stress Response

The psychological stress response was conceptualized as perceived stress in this study. The psychological stress response included perception, appraisal, and coping with situations which the individual encountered. Cohen and his colleagues (1983) first proposed the concept of perceived stress and defined perceived stress as the degree to which an individual appraises events as unpredictable, uncontrollable, and overloading (Cohen et al., 1983). Perceived stress is based on the relationship between the person and the environment. Cohen (1983) developed a global and event-specific measure of perceived stress which is based on how individuals perceive or evaluate a situation as stressful or not stressful (Cohen et al., 1983; Cohen & Williamson, 1988).

In this study, perceived stress was defined as how men with localized prostate cancer following radical prostatectomy or radiation therapy perceived or evaluated the situation/environment as stressful or not stressful. Example of stressful situations included the treatment modalities, symptoms, and symptom distress. The Perceived Stress Scale (PSS) was used to measure the degree of stress experienced by patients with localized prostate cancer receiving radical prostatectomy or radiation therapy.

#### *Measures: Perceived Stress Scale*

The Perceived Stress Scale (PSS) was designed to measure the degree to which situations in one's life are appraised as stressful. The Perceived Stress Scale has been demonstrated to possess substantial reliability and validity. The PSS demonstrated adequate reliability ( $\alpha = 0.84 \sim 0.86$ ) and concurrent validity with measures of depressive



symptoms, anxiety and life event scores (Cohen et al., 1983; Cohen & Williamson, 1988).

The original Perceived Stress Scale was a 14-item measure of the general appraisal of stressful situations in one's life (Cohen et al., 1983). More recently, normative data on the 10-item PSS showed good psychometric properties ( $\alpha = 0.90$ ;  $r = 0.80$ ) and was recommended over the 14-item measure (Cohen & Williamson, 1988). Items are rated on a 5-point frequency scale ranging from 0 to 4. For each question, the participant was asked to indicate on a scale from 0 (never) to 4 (very often) how often they felt or thought about certain situation during the past week (i.e. In the past week, how often have you felt that you were unable to control the important things in your life? How often have you felt nervous and stressed?). Higher scores on the PSS indicated greater perceived stress. The 10-item Perceived Stress Scale is included in Appendix D.

**Aim Two:** To describe the severity and frequency of symptoms and the degree of symptom distress in men with localized prostate cancer following radical prostatectomy or radiation therapy.

#### Measurement of Symptoms and Symptom Distress

Symptoms and symptom distress can be measured by self-report tools (Rhodes & Watson, 1987). The Symptom Indexes was used to measure symptoms and symptom distress in this study. The validity and reliability of the Symptom Indexes has been established and has been appropriately used with patients with early stage prostate cancer following treatment (Clark & Talcott, 2001).

*Measures: The Symptom Indexes*

The Symptom Indexes was developed by Clark and Talcott (2001) and focused on symptoms of dysfunction in four domains—urinary problems, sexual dysfunction, bowel problems, and symptom related distress (Clark & Talcott, 2001). These indexes included disease specific symptoms and symptom distress related to men treated with early stage prostate cancer.

The Symptom Indexes is a 22-item measure of the symptoms (urinary problems, sexual dysfunction, and bowel problems) and symptoms related distress in the past week. In the urinary problems domain, three items assess the degree of urinary incontinence and five items assess urinary obstruction/irritation. Six items assess bowel symptoms (diarrhea, urgency of bowel movements, pain, bleeding, and passing mucus during bowel movements abdominal cramping and tenesmus) associated with treatment. Five sexual dysfunction items focus on physical experience of erections, ejaculation, orgasm, difficulty in getting and keeping erections, and ability to ejaculate and reach orgasm. In addition, parallel items assess symptom distress related to urinary, sexual, and bowel problems. Each item was rated on a 5-point frequency scale ranging from 1 = not at all to 5 = very frequently (Clark & Talcott, 2001).

Each domain of Symptom Indexes is highly correlated. The urinary incontinence index had an acceptable Cronbach's alpha ( $\alpha = 0.86$ ), item-index convergence, and divergence from the urinary obstruction/irritation index. The sexual dysfunction index was internally consistent, although item-index convergence correlations varied somewhat from alphas of 0.67 to 0.89. The bowel function index also had a good internal

consistency ( $\alpha = 0.80$ ) (Clark & Talcott, 2001). The Symptom Indexes is attached in Appendix E.

**Aim Three:** To describe the frequency of strategies for symptom self-management and their perceived effectiveness among men with localized prostate cancer following radical prostatectomy or radiation therapy.

#### Measurement of Symptom Self-Management

Symptom self-management was measured by The Strategy and Effectiveness of Symptom Self-Management (SESSM) questionnaire (Hsiao, 2006). This instrument was developed by the investigator to measure 1) the frequency of symptom self-management strategies and 2) the perceived effectiveness of strategies used by men with localized prostate cancer following radical prostatectomy or radiation therapy.

No instruments for measuring symptom management and self-management related to men treated with prostate cancer were identified in the literature. Descriptive phenomenology has been used to develop particular instruments for symptom management for HIV/AIDS (Bunch, 2004; Fu et al., 2004; Fuller et al., 2005; Tasi et al., 2002). One study developed semi-structured and open-ended questions to obtain 1) examples of symptoms experienced by individuals, 2) descriptions of the symptoms, 3) scores of symptom intensity ranging from 1 (low) to 10 (very high), 4) strategies for symptom management, and 5) assessment of the effectiveness of strategies used to alleviate symptoms (Bunch, 2004; Tasi et al., 2002). This investigator developed the instrument of The Strategy and Effectiveness of Symptom Self-Management (SESSM) questionnaire to measure the frequency of symptom self-management strategies and the

effectiveness of each strategy used by men with localized prostate cancer following radical prostatectomy or radiation therapy.

*Measures: The Strategy and Effectiveness of Symptom Self-Management (SESSM)*

Symptom self-management was measured with the Strategy and Effectiveness of Symptom Self-Management Questionnaire. The Strategy and Effectiveness of Symptom Self-Management is a semi-structural questionnaire which includes the strategies and perceived effectiveness of three main symptoms (urinary incontinence, sexual dysfunction, and bowel problem) among men with localized prostate cancer receiving radical prostatectomy or radiotherapy.

The Strategy and Effectiveness of Symptom Self-Management (SESSM) was created based on information from a systematic literature review on symptom management in prostate cancer and diseases such as HIV/AIDS and other chronic diseases. Content validity was established through consultation with individuals who were experts in the management of symptoms among men with localized prostate cancer. The questionnaire was reviewed by prostate cancer nursing specialists and practitioners, oncologists and members of the prostate cancer social support group in the Arizona Cancer Center at UMC in Tucson.

The SESSM questionnaire consisted of 2 subscales, the strategies to alleviate symptoms (urinary problems, bowel problems, and sexual dysfunction) and the perceived effectiveness of each strategy used. Symptoms of urinary problems included leaking urine, slow or difficult urine flow, urination at night, frequent urination, pain or burning during urination, and urgency in urination. For each urinary symptom, five to six

strategies listed in the questionnaire (i.e. use pad, take medicines, decrease social activities, or endure). For bowel problems, there were four symptoms related to bowel problems, and three to ten strategies for each symptom were included in the questionnaire (i.e. massage, rest, not eat, or take medicines). For sexual dysfunction, nine to ten strategies (i.e. express feeling with partner, find alternative ways such as hugging, kissing, or decrease frequency of sexual activity) were included in the SESSM questionnaire.

Participants were asked to rate the frequency of using a symptom self-management strategy (from 0 to 3; 0 = never use, 1 = seldom use, 2 = moderately use, 3 = use everyday). If there was no applicable strategy then participants could add the strategies they used to manage their symptoms. Participants were then asked to rate the perceived effectiveness of each of the strategies they used (from 0 to 3; 0 = not at all, 1 = slightly, 2 = moderately, 3 = extremely). The Strategy and Effectiveness of Symptom Self-Management Questionnaire is included in Appendix F. Table 2 summarizes the study variables and measures, the validity and reliability of the instrument, and the schedule for collecting data.

Table 2.

*Summary of Study Variables and Measures*

Variable (Study Aims)	Study Measures	Validity/Reliability	Data Collection Schedule
Physiological stress response: salivary cortisol (Aim One)	Salimetrics HS High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit (Salimetrics, 2007)	Sensitivity: .007ug/dL. Intra-assay coefficients: between 3.9% and 7.1% inter-assay coefficients: between 6.7% and 6.9%	1-3 months after radical prostatectomy or 1 <sup>st</sup> radiation therapy
Psychological stress response: perceived stress (Aim One)	Perceived Stress Scale (PSS) (Cohen, 1983)	Internal consistency ( $\alpha = 0.90$ ; $r = 0.80$ )	
Symptom experience: symptoms and symptom distress (Aim Two)	Symptom Indexes (SI) (Clark & Talcott, 2001)	Internal consistency ( $\alpha = 0.86 \sim 0.89$ )	
Outcomes: the frequency of strategies and perceived effectiveness of symptom self- management (Aim Three)	Strategy and Effectiveness of Symptom Self- Management (SESSM) questionnaire (Hsiao, 2006)	Systematic literature review Content validity Experts consultation	

## Data Collection

### Recruitment

Following human subjects approval, participants were recruited from (1) urology clinics and the Department of Radiology Oncology in the Arizona Cancer Center at the University Medical Center and the Southern Arizona Veterans Affairs Health Care System, (2) community based urology clinics, and (3) Prostate Cancer Support Groups in Tucson Arizona. Participants were introduced to the study via flyers posted in the clinics or given to them by their physician or the researcher (PI) during follow up visits to the clinics. The flyer included the title of the study, the inclusion criteria, and contact information. The study flyer is attached in Appendix F.

### Procedure

The Investigator conducted face-to-face interviews with participants between 1 and 3 months after the radical prostatectomy or the first radiation therapy. The researcher met each participant at the outpatient unit in the hospital or at his home. The investigator then introduced the study and informed consent was obtained before collecting data from each participant. To engage patients in the data collection process and to provide a full opportunity to avoid ambiguous or confusing items, items were read aloud and oral responses were recorded.

After signing the consent form, participants were asked to fill out the Demographics Questionnaire that requested information about age, ethnic background, education, marriage, income, and medical history such as date of diagnosis, treatment

modalities, and PSA levels at diagnosis age were included. The Demographics Questionnaire is included in Appendix G.

At the end of interview, participants were given a package to take home which included the supplies for collecting saliva samples (16 cotton swabs and 8 special plastic tubes labeled with a color coded sticker), the study protocol for collecting saliva samples (Appendix A), the schedule for saliva sample collections (4 time points, 6:00-7:00, 11:00-12:00, 16:00- 17:00 and 21:00-22:00, on two consecutive days, Appendix H), a daily log on collecting saliva samples (Appendix I), and 3 questionnaires (Perceived Stress Scale, the Symptom Indexes, and the Strategy and Effectiveness of Symptom Self-Management Questionnaire). The interviews generally required approximately 30 minutes. To minimize dropout, a Chinese charm was given as a small incentive upon completion of the surveys.



## Data Preparation

### Physiological Measure-Salivary Cortisol

Salivary cortisol was used as a physiological marker of stress in this study. Saliva samples were collected with a sorbette according to the manufacturer's instructions and stored in a conical tube before centrifuging. The sorbette was a small triangular-shaped absorbent sponge attached to a plastic shaft. It was non-toxic and super-absorbent, making it the ideal saliva collection device for special populations (infants, toddlers, elderly or under any situation where choking is a concern). All samples were assayed for blood contamination using Salimetrics' Salivary Blood Contamination Enzyme Immunoassay (CN 1-1302/1-1312, 96-Well Kit; Salimetrics, Inc., State College, PA) to rule out contamination of the saliva with blood (Salimetrics, 2007). There is no significant difference in cortisol concentrations between saliva samples with a small amount of blood contamination and those without blood contamination, so all saliva samples were used to assay salivary cortisol.

Four hundred twenty-four saliva samples were assayed for salivary cortisol in duplicate using Salimetrics HS High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit (CN 1-3002/1-3012, 96-Well Kit; Salimetrics, Inc., State College, PA) (Salimetrics, 2007). Salivary cortisol levels were determined in ug/dL by calculating the mean of duplicate assay results. One subject had 1 missing saliva sample. Fourteen of 64 samples obtained from 8 subjects had insufficient volume for duplicate assays. A proxy cortisol level was used for data analysis by replacing the missing cortisol level with the cortisol value from another day. The insufficient saliva samples were diluted with 0.9% saline

before completing the cortisol assay. Overall cortisol levels were measured for day 1, day 2 and 2-day diurnal mean levels. The quantitative measurement of cortisol in saliva was performed using an enzyme-linked immunoabsorbent technique (ELISA) according to the manufacture's instructions and procedures (Salimetrics, 2007). The ELISA micro-plate was coated with monoclonal antibodies to cortisol. The reaction produced a color that was measured at 450 nm on the GENios Tecan plate reader. The intensity of the color reflected the amount of cortisol present (Haussmann, Vleck, & Farrar, 2007).

The area under the curve (AUC) represented the total amount of cortisol secreted throughout the day (from the awakening to bedtime). Two types of AUC provide different information about cortisol secretion: area under the curve with respect to ground (AUCg) and area under the curve with respect to increase (AUCi). AUCg is the total area under the curve of all measurements, and it takes into account sensitivity and intensity. AUCi is calculated with reference to the baseline measurement and it ignores the distance from zero for all measurements.

The average area under the curve (AUC) was calculated over the 2 days of sample collection by trapezoidal estimation using both raw cortisol values and log transformed cortisol values (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). Then the differences between raw and log transformed values were compared. The formulas were:

$$AUCg = t_1 (m_1+m_2)/2 + t_2 (m_2+m_3)/2 + t_3 (m_3+m_4)/2$$

$$AUCi = [t_1 (m_1+m_2)/2 + t_2 (m_2+m_3)/2 + t_3 (m_3+m_4)/2] - (n-1) \cdot m_1$$

Where  $m$  = the individual measurement;  
 $t$  = the distance between measurement;  
 $n$  = the total number of measurements

In addition, circadian rhythm was measured by individual linear regression. The slope of the regression line predicting cortisol level from time of day was used to represent each participant's diurnal cycle of cortisol. Since the distribution of raw cortisol values was positively skewed and the normal diurnal profile may be approximated by an exponential curve, raw values were log transferred prior to analysis. The regression of the 8 cortisol values on the hour of sample collection was calculated, with data pooled over the 2 days for each participant. Circadian rhythm/diurnal cycles were estimated from 4 time points (6:00-7:00, 11:00-12:00, 16:00-17:00, and 21:00-22:00) across 2 days.

### Data Analysis

Descriptive statistics (such as measures of central tendency, mean, standard deviation, range, and skewness/symmetry) were used to describe sample characteristics including the number of men in the sample who received radical prostatectomy vs. radiation therapy, the average amount and variation in salivary cortisol, perceived stress, symptoms, symptom distress, and symptom self-management. Statistical Package for the Social Sciences (SPSS 15.0) for windows was used to execute data analysis in this study (Field, 2005).

Each variable was examined to meet the assumptions of Pearson Product Moment Correlation and regression analysis including 1) normal distribution, 2) homoscedasticity, and 3) linearity. If a variable was not linear, transformations were made and described prior to conducting correlational and regression analyses. Pearson Product Moment Correlation analysis was used to address bivariate correlation, and multiple linear regression was used to determine if salivary cortisol, perceived stress, symptoms, and symptom distress were significant predictors of symptom self-management strategies in men treated with localized prostate cancer. The data analysis plan for each study aim and related research questions is summarized below.

**Aim One:** To examine physiological and psychological stress responses in men with localized prostate cancer following radical prostatectomy or radiation therapy.

**Research Questions:**

1-a. What are the levels and circadian patterns of the physiological stress response measured by salivary cortisol? Are there any differences between the two subgroups?

The physiological stress response was measured by salivary cortisol. Levels of cortisol were measured in  $\mu\text{g/dL}$ . The mean and standard deviation of duplicate assays at 4 time periods (awaking, morning, afternoon, and evening) each day for 2 days were calculated. An overall mean, standard deviation and range were calculated for salivary cortisol concentrations. To describe the circadian pattern of cortisol secretion, mean salivary cortisol levels were graphed by day and time interval. The individual regression of the 8 cortisol values was calculated from 4 data collection time points over 2 days. The slope ( $\beta$ ) of the regression line predicting cortisol level from time of day was used to represent each participant's circadian rhythm of cortisol.

1-b. What are the levels of the psychological stress response as measured by the Perceived Stress Scale? Are there any differences between the two subgroups?

An overall mean, standard deviation and range were used to describe levels of perceived stress and a t-test was used to determine if there were any differences in PSS between the two groups of men with prostate cancer treated with either radical prostatectomy or radiation therapy.

1-c. What is the relationship between the physiological stress response (salivary cortisol) and the psychological stress response (perceived stress) among men with localized prostate cancer following radical prostatectomy or radiation therapy?

A Pearson Product correlation was computed to examine the strength and direction of the relationship between salivary cortisol and perceived stress.

**Aim Two:** To describe the severity and frequency of symptoms and the degree of symptom distress experienced by men with localized prostate cancer following radical prostatectomy or radiation therapy.

**Research Questions:**

2-a. What levels of symptoms (severity and frequency) do men with localized prostate cancer following radical prostatectomy or radiation therapy experience?

2-b. What is the degree of symptom distress among men with localized prostate cancer following radical prostatectomy or radiation therapy?

Means, standard deviations and ranges were calculated to describe the severity and frequency of symptoms and the degree of symptom related distress. Composite scores for symptoms and symptom distress were computed according to Clark and Talcott's instruction (Clark & Talcott, 2001).

2-c. What is the relationship between symptoms and symptom distress among men with localized prostate cancer following radical prostatectomy or radiation therapy?

A Pearson Product correlation was computed to examine the strength and direction of the relationship between symptoms and symptom distress.

**Aim Three:** To describe symptom self-management strategies and perceived effectiveness among men with localized prostate cancer following radical prostatectomy or radiation therapy.

**Research Questions:**

3-a. What is the frequency of strategies for symptom self-management used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

3-b. What is the perceived effectiveness of each strategy used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

Descriptive statistics were used to describe the frequency and the effectiveness of strategies used by patients to alleviate their symptoms associated with urinary problems, bowel problems, and sexual dysfunction.

3-c. What is the relationship between the frequency of using a strategy to alleviate symptoms and the perceived effectiveness of each strategy used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

A Pearson Product correlation was computed to examine the strength and direction of the relationship between the frequency of using a strategy to alleviate symptoms (urinary problems, bowel problems, and sexual dysfunction) and the perceived effectiveness of each strategy used.

**Aim Four:** To examine the relationships among stress (physiological and psychological responses), symptoms, symptom distress and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy.

**Research Questions:**

4-a. What are the relationships among stress, symptoms, symptom distress, and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy?

Pearson Product Moment Correlations were used to examine the strength and direction of the relationships among stress, symptoms, symptom distress, and symptom self-management.

4-b. To what extent does stress (salivary cortisol and perceived stress) predict symptoms and symptom distress among patients with localized prostate cancer following radical prostatectomy or radiation therapy?

A multiple regression analysis was used to determine if salivary cortisol and perceived stress were significant predictors of the symptoms and symptom distress.

4-c. To what extent does stress (salivary cortisol and perceived stress) predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

A multiple regression analysis was used to determine if salivary cortisol and perceived stress were significant predictors of the frequency of symptom self-management strategies, and a multiple linear regression was performed.

4-d. To what extent do symptoms and symptom distress predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

A multiple regression analysis was used to determine if symptoms and symptom distress were significant predictors of the frequency of symptom self-management strategies.

4-e. To what extent do stress (salivary cortisol and perceived stress), symptoms, and symptom distress predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

A hierarchical linear regression was used to determine if salivary cortisol, perceived stress, symptoms, and symptom distress were significant predictors of



symptoms self-management strategies. Furthermore, a stepwise multiple regression was conducted to explore the largest and significant predictors of the frequency for symptom self-management strategies.

### Summary

A cross-sectional, descriptive, and correlational research design was used in this study. Descriptive statistics, Pearson Product Moment Correlations, and multiple linear and hierarchical regressions were used to analyze the psychometrics data. Salivary cortisol was assayed by an enzyme-linked immunoabsorbent technique (ELISA) and measured at 450 nm on the GENios Tecan plate reader. All data were analyzed by Statistical Package for the Social Sciences (SPSS version 15.0) for windows. In this study, a power of 0.80, an alpha ( $\alpha$ ) of 0.05, and a moderate effect size of 0.13 were selected. The estimated sample size in this study was between 50 to 77. Data preparation and data analysis for each study aim and research question were discussed.

## CHAPTER IV

### RESULTS OF DATA ANALYSIS

#### Introduction

The purpose of this study was to investigate relationships among stress, symptoms and symptom distress, and symptom self-management in patients with localized prostate cancer following radical prostatectomy and/or radiation therapy. The measures of stress, symptoms and symptom distress and symptom self-management included the Perceived Stress Scale, the Symptom Indexes and the Strategy and Effectiveness of Symptom Self-Management Questionnaire. Salivary cortisol was used as a biological measure of stress. A second purpose was to identify effective strategies for symptom self-management among patients with localized prostate cancer following radical prostatectomy and/or radiation therapy. The results will be presented in the following sections: (1) description of the study setting and sample, (2) reliability of the instruments, (3) findings related to study aims and research questions.

#### Description of the Setting and Sample

##### Setting

Participants were recruited from two medical centers, three private urology clinics, and three Prostate Cancer Support Groups in Tucson Arizona. Eighty-seven percent of the participants ( $n = 46$ ) were recruited from Radiology Oncology at the University of Arizona Medical Center and the Urology Clinic at the Southern Arizona Veterans Affairs Health Care System in Tucson. Ten percent of the participants ( $n = 5$ ) were recruited from community-based Urology Clinics and Radiology Oncology Clinics

in Tucson. Three percent of the participants ( $n = 2$ ) were recruited from Prostate Cancer Support Groups in Tucson.

### Sample

The sample consisted of fifty-three men with localized prostate cancer receiving radical prostatectomy and/or radiation therapy. The demographics and characteristics of the sample are shown in Table 3. Fifty-three men with prostate cancer consented to participate in this study. The mean age of the sample was 68 ( $SD = 6.9$ ) years with a range of 52 to 80 years. Eighty-one percent ( $n = 43$ ) of the participants were Caucasian, 9.4% ( $n = 5$ ) were Hispanic/Latin, and 9.4 % ( $n = 5$ ) were African American. The average education of the sample was 16 years. Sixty-eight percent ( $n = 36$ ) of the participants were married. Sixty-four percent ( $n = 34$ ) of the participants reported they were no longer employed. Seventy percent ( $n = 37$ ) of the participants reported “income exceeds my expenses” to the question about their income.

Fifty-five percent ( $n = 29$ ) of the participants received radiation therapy and 45% ( $n = 24$ ) of the participants received radical prostatectomy. The average PSA at the time of diagnosis was 6.51 ng/mL ( $SD = 3.1$ ) with a range of 1.7 to 17 ng/mL. The average length of time between diagnosis and initiation of treatment was 6.51 months ( $SD = 3.10$ ) with a range of 2 to 36 months. The average length of time between beginning prostate cancer treatment and data collection was 43.49 days ( $SD = 16.14$ ) with a range of 28 to 90 days.

Table 3.

*Description of Sample Demographics and Characteristics (n=53)*

	<i>Mean</i>	<i>SD</i>	<i>Range</i>	<i>N</i>	<i>%</i>
Age in years	68.08	6.9	52-80	53	100
Ethnic					
Caucasian				43	81.2
African-American				5	9.4
Hispanic				5	9.4
Education	16.17	3.5	9-24		
Marital status					
Single				4	8
Married				36	68
Divorced				12	22
Widowed				1	2
Income					
Income exceeds my expenses				37	70
Income meets my expenses				14	26
Income barely meets my expenses				2	4
Currently employed					
Yes				19	40
No				34	64
PSA at diagnosis	6.51	3.1	1.7-17		
Time since diagnosis (Month)	7.40	5.8	2-36		
Time since treatment (Day)	43.49	16.1	28-90		
Treatment					
Radical Prostatectomy				24	45
Radiation Therapy				29	55

## Reliability of the Instrument

### Perceived Stress Scale

The internal consistency of the items in the Perceived Stress Scale (PSS) was determined using Cronbach's alpha. The PSS consists of 10 items that assess amount of perceived stress. Participants were asked about their feelings and thoughts over the past week in this study (e.g. "In the past week, how often have you felt that you were unable to control the important things in your life?"). Each item on the PSS was scored on a range of 0-4 with higher total scores indicative of higher stress. Four items were reverse scored. The highest score (most stressed) was 40 and the lowest score (less stressed) was 0. The Cronbach's alpha for the PSS was .838; the standardized alpha was .841. The 10-item PSS showed good psychometric properties.

### Symptom Indexes

The Symptom Indexes (SI) consist of 22 items that assess symptoms of dysfunction in four domains—urinary problems (urinary incontinence, urinary obstruction/irritation), sexual dysfunction, bowel problems, and symptom related distress. Each item was rated on a 5-point frequency scale ranging from 1 = not at all to 5 = very frequently. The internal consistency of the items in the Symptom Indexes was determined using Cronbach's alpha. The Cronbach's alpha for the total Symptom Indexes was .873 (the standardized alpha was .911); for the SI-urinary problems it was .626 (the standardized alpha was .623); for the SI-bowel problems it was .802 (the standardized alpha was .805); for the SI-sexual dysfunction it was .869 (the standardized alpha was .878); and for the SI- symptom related distress it was .877 (the standardized alpha was

.873). The total Symptom Indexes, symptom subscale, and symptom related distress subscale had moderate to high internal reliability; therefore, they showed good psychometric properties.

#### Strategy and Effectiveness of Symptom Self-Management Questionnaire

##### The Strategy and Effectiveness of Symptom Self-Management (SESSM)

questionnaire consists of 140 items. There are two subscales: the frequency of using a strategy to alleviate of symptoms (urinary problems, bowel problems, and sexual dysfunction) and the perceived effectiveness of each strategy that was used. Each item was scored on a range of 0-3 with higher total scores indicating higher frequency and more effectiveness of each strategy that was used. Cronbach's alpha was used to determine the internal consistency of the items in the symptom self-management strategy and effectiveness questionnaire. The Cronbach alpha for the total SESSM was .929 (the standardized alpha was .930). Table 4 presents the Cronbach alpha and the standardized alpha for the two SESSM subscales. The total SSMSE and 2 subscales showed good internal reliability.

Table 4.

##### *Cronbach Alpha of SESSM Questionnaire*

	Total SESSM (140 items)	Strategy (70 items)	Effectiveness (70 items)
Cronbach alpha	.929	.876	.865
Standardized alpha	.930	.882	.866

### Salimetrics Expanded Range High Sensitivity Salivary Cortisol Enzyme Immunoassay

Saliva samples were assayed for salivary cortisol using the Salimetrics HS High Sensitivity Salivary Cortisol Enzyme Immunoassay. The Salimetrics HS High Sensitivity Salivary Cortisol Enzyme Immunoassay has a range of sensitivity from 0.003 µg/dL to 3.0 µg/dL, with serum correlation of 0.96. The intra-assay coefficients of variation were between 3.35 % and 3.65 %. The inter-assay coefficients of variation were between 3.75 % and 6.41 %.

### Salivary Blood Contamination Enzyme Immunoassay

The Salimetrics' Salivary Blood Contamination Enzyme Immunoassay KIT (CN 1-1302/1-1312, 96-Well Kit; Salimetrics, Inc., State College, PA) was used to determine if a saliva sample was contaminated with blood. The sensitivity of the Salimetrics' Salivary Blood Contamination Enzyme Immunoassay was 0.08 mg/dL. The average intra-assay coefficients of variation were 10.2 % and 4.9 %, respectively. The average inter-assay coefficients of variation were 9.0 % for low and 4.1 % for high transferrin levels.

## Findings Related to Study Aim and Research Question

### **Aim One**

To examine physiological and psychological stress responses in men with localized prostate cancer following radical prostatectomy or radiation therapy. There were three research questions.

### **Research Question One**

What are the levels and circadian pattern of the physiological stress response measured by salivary cortisol? Are there any differences between 2 subgroups?

The physiological stress response was assessed by a measure of salivary cortisol. Levels of cortisol were measured in  $\mu\text{g/dL}$  by calculating the mean of duplicate assays. Since the distribution of raw cortisol values was positively skewed, the normal diurnal profile may be approximated by an exponential curve, and to deal with the lack of linearity, raw values were log transformed prior to analysis. To thoroughly understand the data, log transformed data and raw data were both used in data analyses in this study.

Table 5-1 presents the mean values for salivary cortisol concentration using raw data at 4 time points (awakening, noon, afternoon, and evening) on day 1, day 2, and the mean of both days in the total sample and the two subgroups. Table 5-2 presents the mean of salivary cortisol concentrations using log transformed data at 4 time points (awakening, noon, afternoon, and evening) on day 1, day 2, and the mean of both days from the total sample and the two subgroups.



Table 5-1.

*Mean Salivary Cortisol Concentrations\**

Time	Awaking (6-7 am)	Noon (11-12 pm)	Afternoon (4-5 pm)	Evening (9-10 pm)
<i>Day1</i>				
Total Sample (n=53)	0.314 (0.216)	0.158 (0.128)	0.121 (0.157)	0.077 (0.094)
Radical Prostatectomy (n=24)	0.349 (0.255)	0.150 (0.094)	0.075 (0.050)	0.055 (0.044)
Radiation Therapy (n=29)	0.285 (0.178)	0.165 (0.151)	0.159 (0.201)	0.095 (0.119)
<i>Day2</i>				
Total Sample (n=53)	0.302 (0.314)	0.131 (0.153)	0.102 (0.188)	0.082 (0.074)
Radical Prostatectomy (n=24)	0.383 (0.429)	0.116 (0.081)	0.094 (0.118)	0.088 (0.076)
Radiation Therapy (n=29)	0.236 (0.147)	0.144 (0.194)	0.108 (0.232)	0.077 (0.073)
<i>Day1+Day2</i>				
Total Sample (n=53)	0.306 (0.214)	0.144 (0.095)	0.111 (0.117)	0.080 (0.061)
Radical Prostatectomy (n=24)	0.366 (0.277)	0.133 (0.061)	0.085 (0.065)	0.072 (0.043)
Radiation Therapy (n=29)	0.256 (0.127)	0.154 (0.115)	0.133 (0.144)	0.086 (0.072)

\* Means obtained from raw data, n=53

Table 5-2.

*Mean Salivary Cortisol Concentrations\**

Time	Awaking (6-7 am)	Noon (11-12pm)	Afternoon (4-5 pm)	Evening (9-10 pm)
<i>Day1</i>				
Total Sample (n=53)	-1.361 (0.631)	-2.080 (0.681)	-2.575 (0.917)	-3.083 (1.217)
Radical Prostatectomy (n=24)	-1.282 (0.682)	-2.076 (0.617)	-2.856 (0.847)	-3.388 (1.434)
Radiation Therapy (n=29)	-1.427 (0.590)	-2.084 (0.741)	-2.342 (0.922)	-2.831 (0.960)
<i>Day2</i>				
Total Sample (n=53)	-1.509 (0.742)	-2.384 (0.815)	-2.862 (0.979)	-2.965 (1.138)
Radical Prostatectomy (n=24)	-1.399 (0.923)	-2.337 (0.598)	-2.829 (0.963)	-3.016 (1.425)
Radiation Therapy (n=29)	-1.601 (0.551)	-2.422 (0.969)	-2.889 (1.009)	-2.923 (0.857)
<i>Day1+Day2</i>				
Total Sample (n=53)	-1.379 (0.616)	-2.093 (0.555)	-2.543 (0.798)	-2.792 (0.753)
Radical Prostatectomy (n=24)	-1.255 (0.722)	-2.124 (0.471)	-2.719 (0.735)	-2.839 (0.711)
Radiation Therapy (n=29)	-1.482 (0.503)	-2.068 (0.624)	-2.397 (0.831)	-2.753 (0.798)

\* Means obtained from log transformed data, n=53

### *Area Under the Curve*

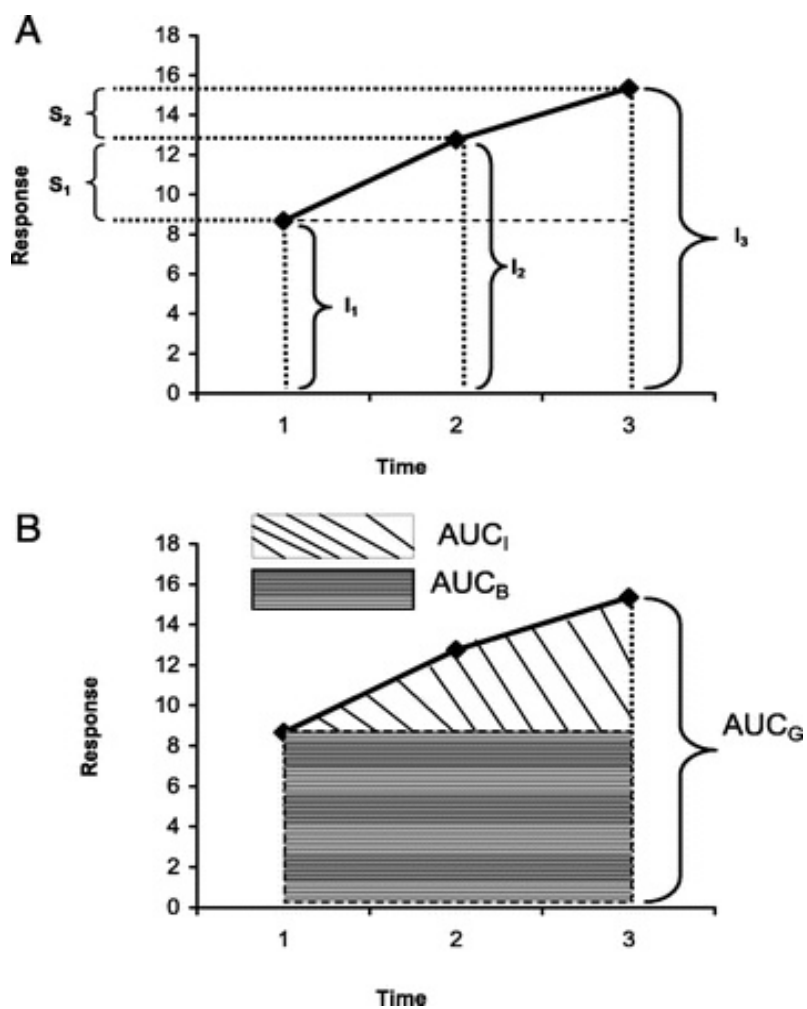
Area under the curve (AUC) represented the total amount of cortisol secreted throughout the day (from the awakening to bedtime). There are two different measures of AUC-area under the curve with respect to ground ( $AUC_G$ ) and area under the curve with respect to increase ( $AUC_I$ ). Area under the curve with respect to ground ( $AUC_G$ ) is the total area under the curve of all measurements.  $AUC_G$  indicates the total cortisol output and it takes into account sensitivity and intensity. The area under the curve with respect to the increased  $AUC_I$  is calculated with reference to the baseline measurement.  $AUC_I$  represents the sensitivity of cortisol and indicates changes over time (Fekedulegn et al., 2007; Pruessner et al., 2003). Figure 5 depicts the area under the curve of salivary cortisol (Fekedulegn et al., 2007).

The formulas for calculating  $AUC_G$  and  $AUC_I$  are  $AUC_G = t_1 (m_1+m_2)/2 + t_2 (m_2+m_3)/2 + t_3 (m_3+m_4)/2$  and  $AUC_I = [t_1 (m_1+m_2)/2 + t_2 (m_2+m_3)/2 + t_3 (m_3+m_4)/2] - (n-1) \cdot m_1$ ; Where  $m$  = the individual measurement;  $t$  = the distance between measurement;  $n$  = the total number of measurements (Pruessner et al., 2003).

Table 6-1 presents the mean salivary cortisol  $AUC_G$  and  $AUC_I$  using raw data on day 1, day 2, and the mean salivary cortisol  $AUC_G$  and  $AUC_I$  of both days from the total sample and the two subgroups. Table 6-2 presents the mean salivary cortisol  $AUC_G$  and  $AUC_I$  using log transformed data on day 1, day 2, and the mean salivary cortisol  $AUC_G$  and  $AUC_I$  of both days from the total sample and the two subgroups.

Figure 5.

*Area Under the Curve (AUC)*



Plot of repeated measurements indicating magnitude of response or intensity ( $I_1$ ,  $I_2$ , and  $I_3$ ) at each time point, changes in the response over time or sensitivity ( $S_1$  and  $S_2$ ) (A) and the three forms of AUC (B). AUC = area under the curve.

*From: Fekedulegn: Psychosom Med, Volume 69(7).September 2007.651-659*

Table 6-1.

*Mean Area Under the Curve of Salivary Cortisol\**

Salivary Cortisol	$AUC_G$ (M/SD)	$AUC_I$ (M/SD)
<i>Day1</i>		
Total Sample (n=53)	2.371 (1.699)	- 2.333 (2.493)
Radical Prostatectomy (n=24)	2.135 (1.188)	- 3.095 (2.869)
Radiation Therapy (n=29)	2.566 (2.028)	- 1.703 (1.967)
<i>Day2</i>		
Total Sample (n=53)	2.125 (1.509)	- 2.412 (4.186)
Radical Prostatectomy (n=24)	2.228 (1.352)	- 3.520 (5.512)
Radiation Therapy (n=29)	2.039 (1.647)	- 1.495 (2.380)
<i>Day1+Day2</i>		
Total Sample (n=53)	2.242 (1.174)	- 2.346 (2.745)
Radical Prostatectomy (n=24)	2.182 (0.962)	- 3.308 (3.439)
Radiation Therapy (n=29)	2.293 (1.339)	- 1.550 (1.681)

\* Means obtained from raw data, n=53

Table 6-2.

*Mean Area Under the Curve of Salivary Cortisol\**

Salivary Cortisol	$AUC_G$ ( $M/SD$ )	$AUC_I$ ( $M/SD$ )
<i>Day1</i>		
Total Sample (n=53)	- 34.382 (9.819)	- 13.967 (8.517)
Radical Prostatectomy (n=24)	- 36.330 (10.293)	- 17.107 (8.220)
Radiation Therapy (n=29)	- 32.770 (9.278)	- 11.368 (7.986)
<i>Day2</i>		
Total Sample (n=53)	- 37.409 (9.109)	- 14.781 (12.852)
Radical Prostatectomy (n=24)	- 36.862 (9.033)	- 15.884 (15.032)
Radiation Therapy (n=29)	- 37.861 (9.305)	- 13.868 (10.920)
<i>Day1+Day2</i>		
Total Sample (n=53)	- 33.606 (7.838)	- 12.919 (9.290)
Radical Prostatectomy (n=24)	- 34.449 (7.468)	- 15.623 (9.762)
Radiation Therapy (n=29)	- 32.908 (8.196)	- 10.681 (8.400)

\* Means obtained from log transformed data, n=53

### *Circadian Rhythm*

Circadian rhythm was measured by individual linear regression. The individual regression of the eight cortisol values was calculated from 4 data collection time points (6:00-7:00, 11:00-12:00, 16:00-17:00, and 21:00-22:00) over 2 days. The slope ( $\beta$ ) of the regression line predicting cortisol level from time of day was used to represent each participant's circadian rhythm of cortisol (Smyth et al., 1997). The smaller negative value of  $\beta$  indicate cortisol is rapidly declining, whereas the larger negative value of  $\beta$  may indicate slower declines in cortisol, having irregular timed peaks, or increasing cortisol level during the day (Sephton et al., 2000).

Figure 6-1 shows the circadian rhythm of salivary cortisol based on means obtained from raw data on day 1, day 2, and the mean of both days for the entire sample. Figure 6-2 shows the circadian rhythm of salivary cortisol based on means obtained from log transformed data on day 1, day 2, and the mean of both 2 days for the entire sample. The slope ( $\beta$ ) of salivary cortisol was -.726 on day 1, -.561 on day 2, and -.644 across both days. The slope ( $\beta$ ) of the log transformed salivary cortisol was -.748 on day 1, -.564 on day 2, and -.656 across both days. Figure 7-1 shows the mean value for salivary cortisol circadian rhythm in the prostatectomy group on day 1 ( $\beta = -.921$ ), day 2 ( $\beta = -.823$ ), and the mean of both days ( $\beta = -.976$ ) from the raw data. Figure 7-2 shows the log transformed mean value for salivary cortisol circadian rhythm in the prostatectomy group on day 1 ( $\beta = -.993$ ), day 2 ( $\beta = -.867$ ), and the mean of both days ( $\beta = -.924$ ). Figure 8-1 shows the mean value for salivary cortisol circadian rhythm in the radiation therapy group on day 1 ( $\beta = -.938$ ), day 2 ( $\beta = -.962$ ), and the mean of both days ( $\beta = -.950$ ) from

raw data. Figure 8-2 shows the log transformed mean value for salivary cortisol circadian rhythm in the radiation therapy group on day 1 ( $\beta = -.959$ ), day2 ( $\beta = -.981$ ), and the mean of both days ( $\beta = -.872$ ).



Figure 6-1.

*Circadian Rhythm in Total Sample Based on Raw Date (n=53)*

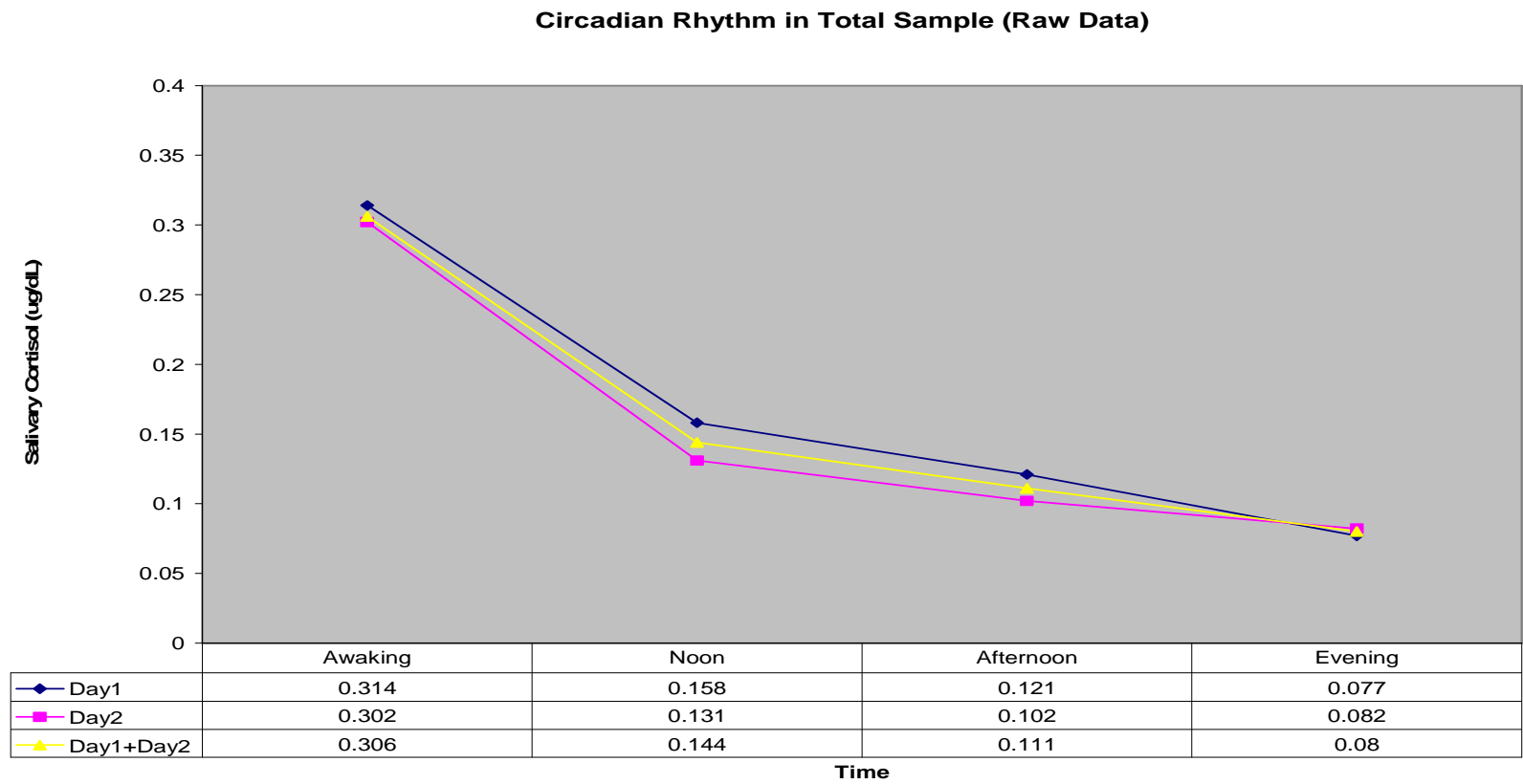


Figure 6-2.

*Circadian Rhythm in Total Sample Based on Log Transformed Data (n=53)*

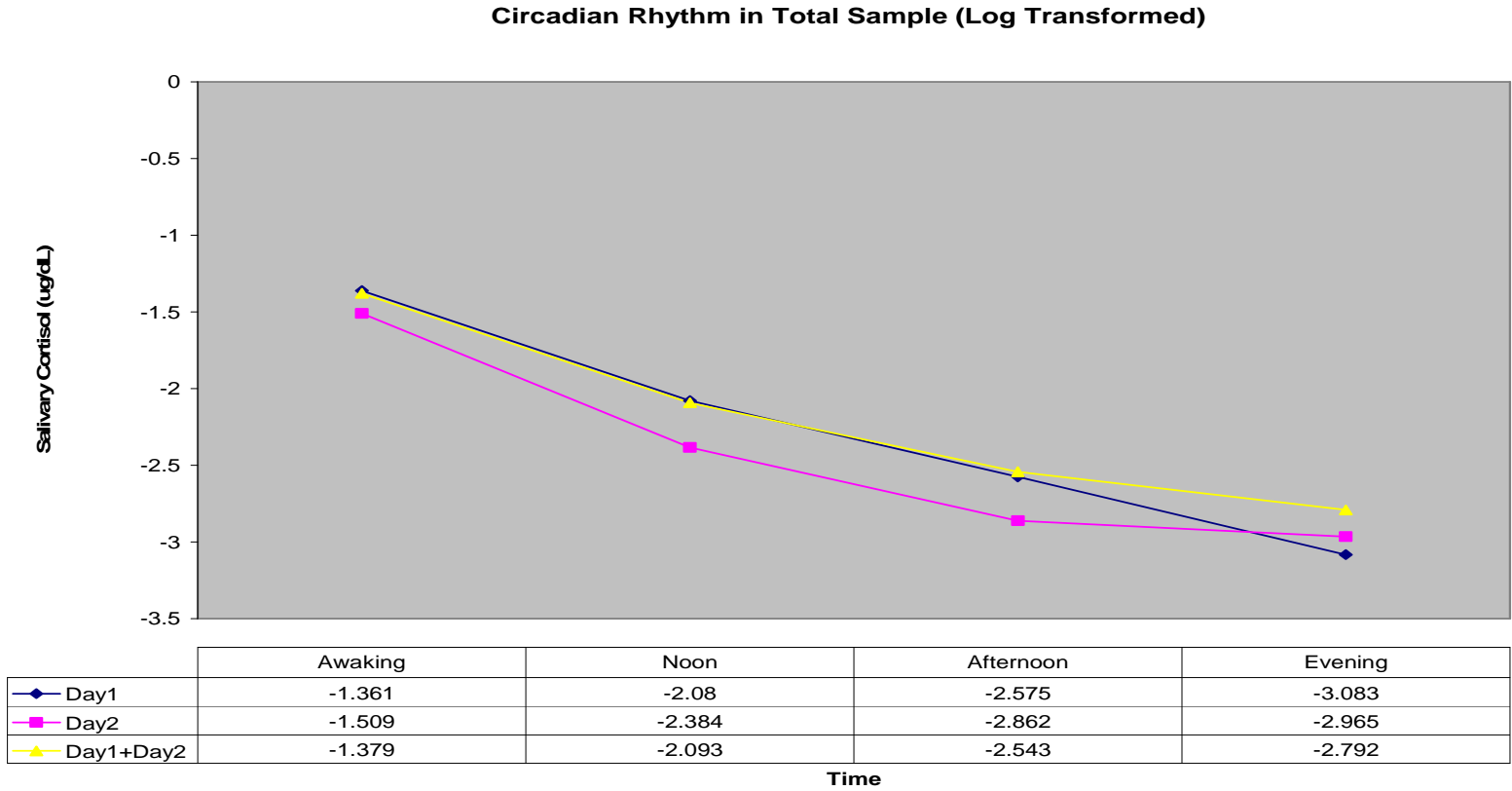


Figure 7-1.

*Circadian Rhythm in Prostatectomy Group Based on Raw Data (n=24)*

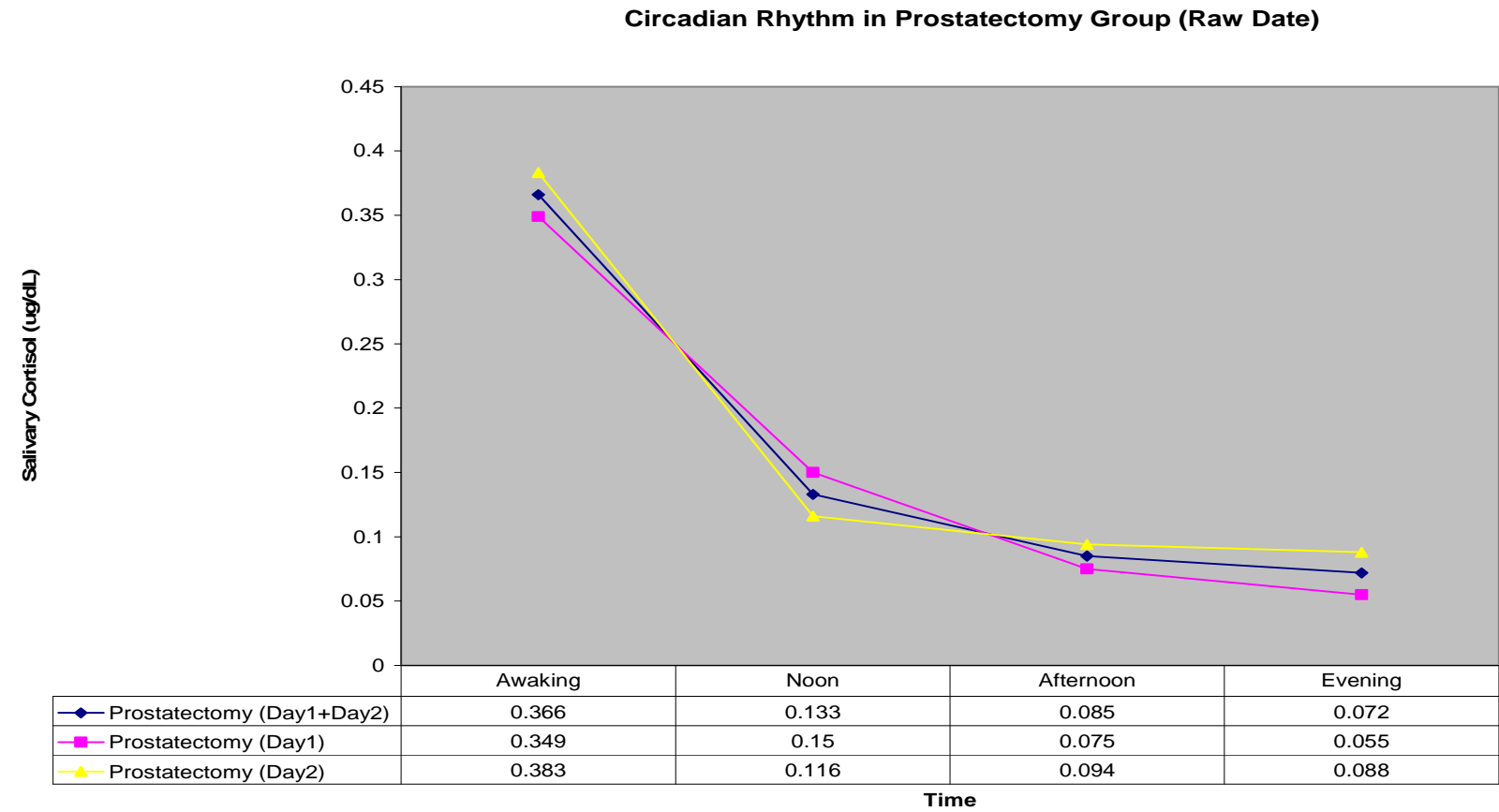


Figure 7-2.  
*Circadian Rhythm in Prostatectomy Group Based on Log Transformed Data (n=24)*

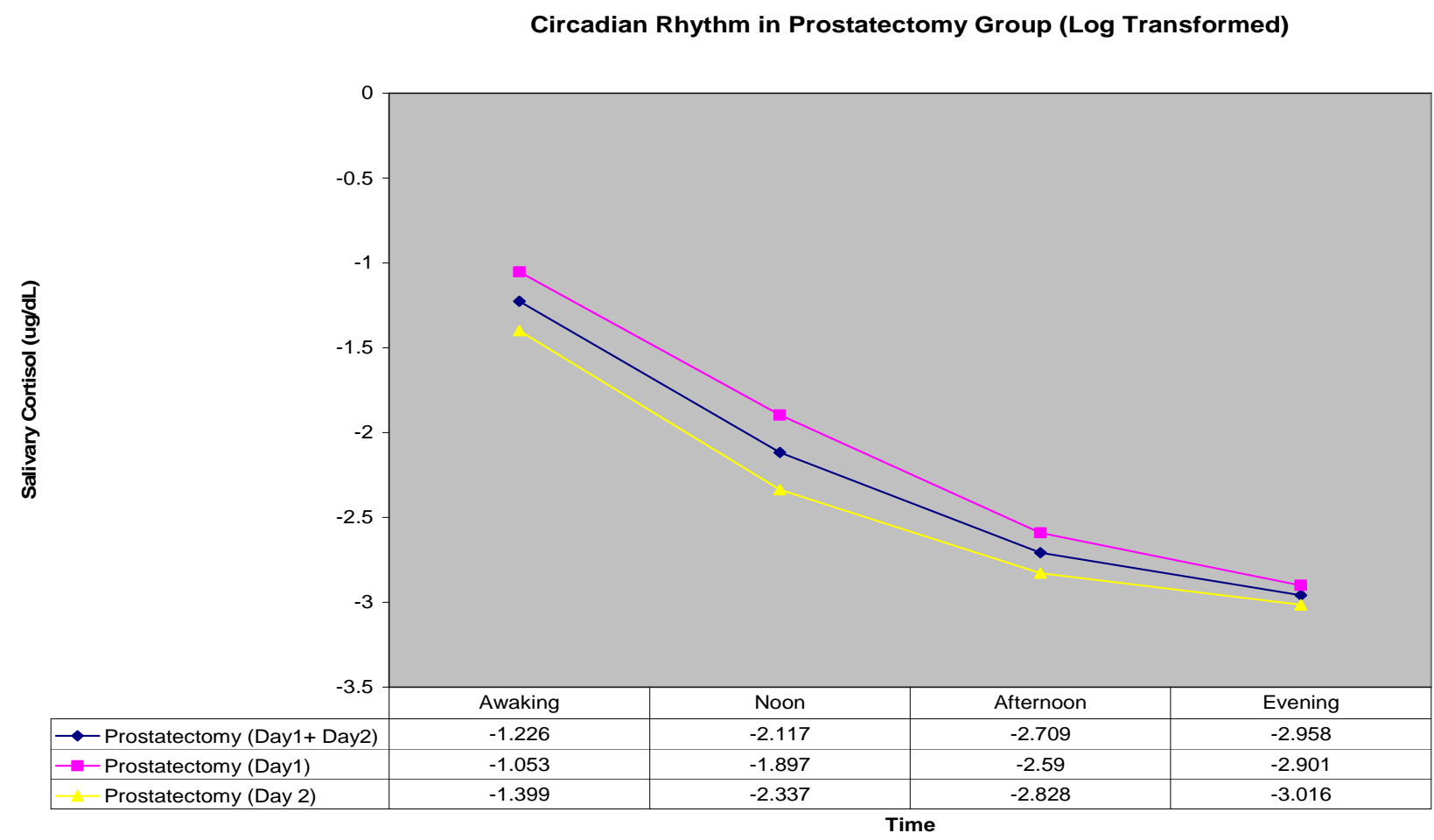


Figure 8-1.

*Circadian Rhythm in Radiation Therapy Group Based on Raw Data (n=29)*

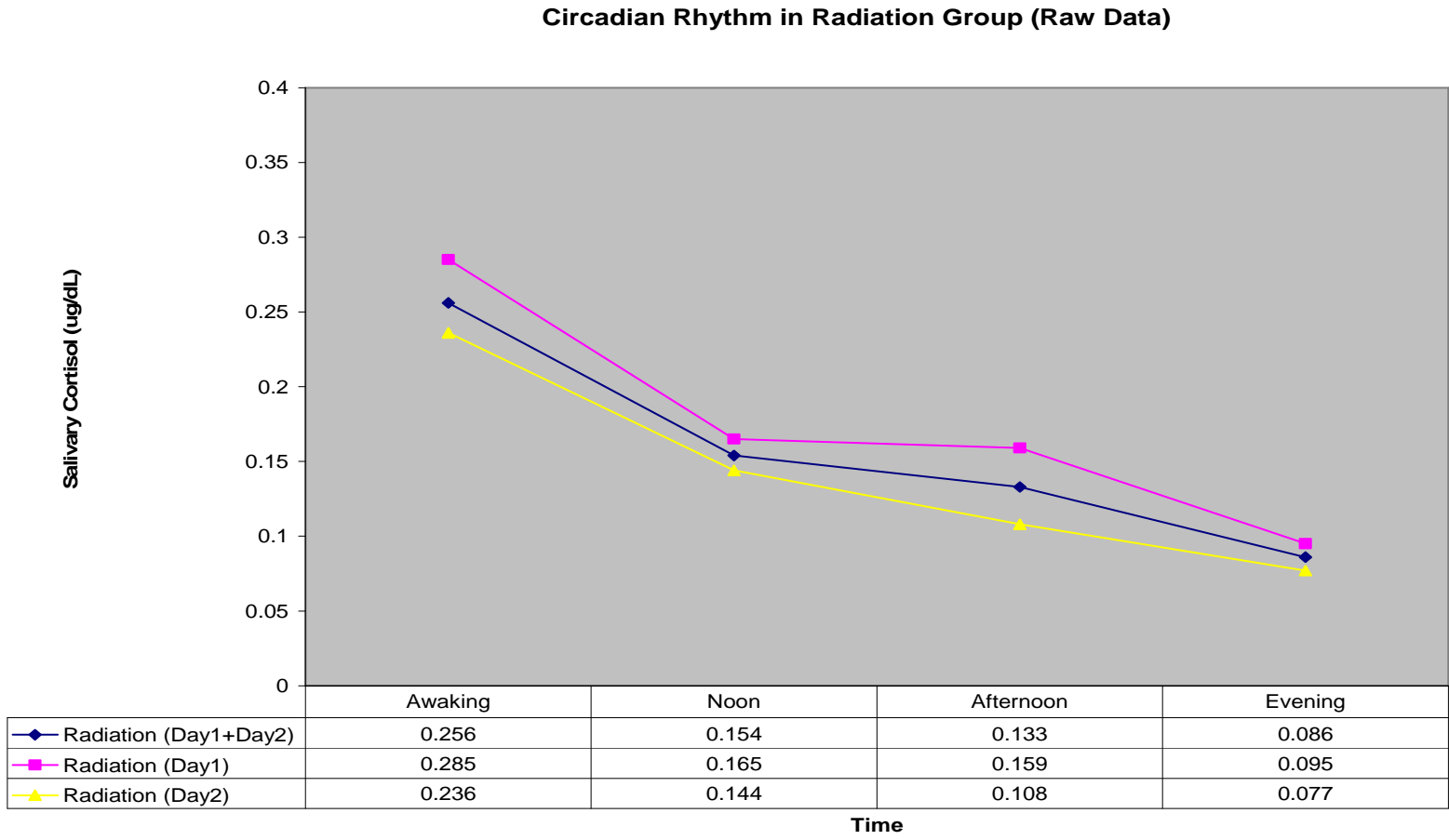
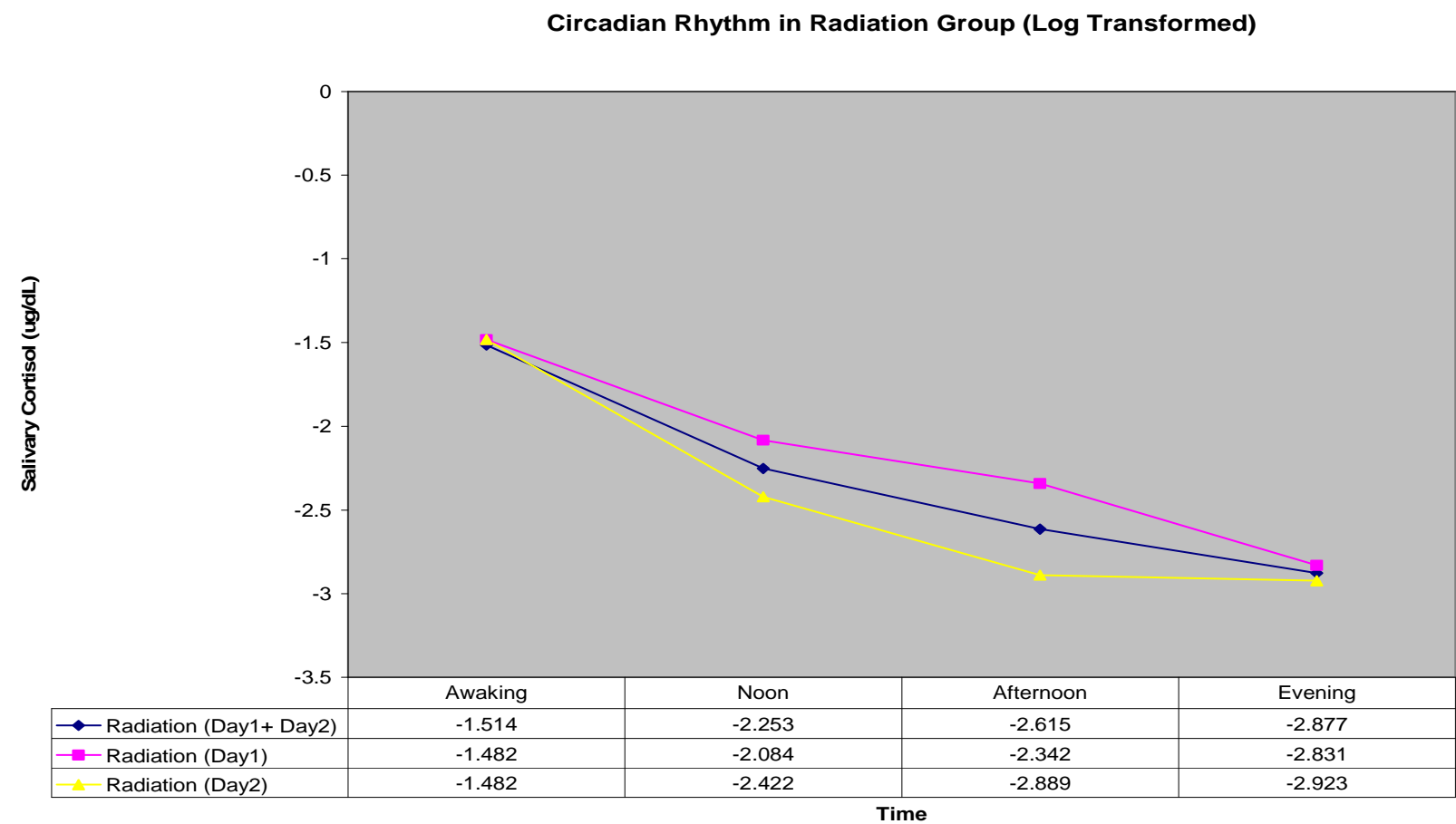


Figure 8-2.

*Circadian Rhythm in Radiation Therapy Group Based on Log Transformed Data (n=29)*



*Salivary Cortisol Indices ( $AUC_G$ ,  $AUC_I$  and  $\beta$ ) in Two Subgroups*

Tables 7-1 and 7-2 summarize the mean salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and Slope) over 2 days in prostatectomy and radiation therapy groups based on raw data and log transformed data. As is generally true across these analyses, the raw data and log transformed data show quite similar findings. The mean salivary cortisol  $AUC_G$ ,  $AUC_I$  and slope ( $\beta$ ) of the radiation therapy group were ( $M = 2.292$ ,  $SD = 1.33$ ,  $M = -1.550$ ,  $SD = 1.68$ ,  $M = -0.624$ ,  $SD = 0.26$  respectively) greater than the radical prostatectomy group ( $M = 2.181$ ,  $SD = 0.96$ ;  $M = -3.301$ ,  $SD = 3.43$ ,  $M = -0.667$ ,  $SD = 0.32$ ), but not reach statistically significant. Only the difference in salivary cortisol  $AUC_I$  based on log transformed data was significant between the subgroups.

Table 7-1.

*Mean  $AUC_G$ ,  $AUC_I$ , and Slope ( $\beta$ ) over 2 days in Subgroups (Raw Data)*

	Radical Prostatectomy (n=24)	Radiation Therapy (n=29)	<i>t</i>	<i>p</i>
Salivary Cortisol Indices	Mean (SD)	Mean (SD)		
$AUC_G$	2.181 (0.96)	2.292 (1.33)	-0.34	0.73
$AUC_I$	-3.301 (3.43)	-1.550 (1.68)	-2.28	0.29
Slope ( $\beta$ )	-0.667 (0.32)	-0.624 (0.26)	-0.52	0.60

Table 7-2

*Mean  $AUC_G$ ,  $AUC_I$ , and Slope ( $\beta$ ) over 2 days in Subgroups (Log Transformed Data)*

	Radical Prostatectomy (n=24)	Radiation Therapy (n=29)	<i>t</i>	<i>p</i>
Salivary Cortisol Indices	Mean (SD)	Mean (SD)		
$AUC_G$	-34.449 (7.46)	-32.908 (8.19)	-0.71	0.48
$AUC_I$	-15.623 (9.76)	-10.681 (8.40)	-1.98	0.05
Slope ( $\beta$ )	-0.683 (0.33)	-0.634 (0.27)	-0.59	0.55



### *Different Patterns of Circadian Rhythm*

Previous studies have identified that three patterns of cortisol circadian rhythm have been identified: typical negative circadian rhythm, non-typical flat circadian rhythm, and inconsistent circadian rhythm (Ice, Katz-Stein, Himes, & Kane, 2004; Smyth et al., 1997; Stone et al., 2001). Smyth et al. (1997) concluded that typical negative and non-typical flat circadian rhythms were identified from the consistent circadian rhythm group. The consistent circadian rhythm (typical negative or non-typical flatten) was defined as cortisol rhythms (the slope) that were highly similar over the 2 days (Smyth et al., 1997). A typical negative circadian rhythm was defined as decreasing cortisol levels over the course of the day. A non-typical flat circadian rhythm was a flat pattern with no decline, the slopes approaching zero. The inconsistent circadian rhythm had variable patterns across two days (Ice et al., 2004; Smyth et al., 1997; Stone et al., 2001).

To determine the circadian rhythm of salivary cortisol, the slope of the regression line was plotted from 4 cortisol values per day over 2 days for each sample. Prior to identifying whether there was a typical circadian rhythm (typically negative rhythm) or a non typical circadian rhythm (flat rhythm), the consistency of the circadian rhythm over 2 days had to be established.

In order to evaluate the consistency of the circadian rhythm between 2 days, individual linear regressions were calculated. Two individual linear regressions were conducted to generate the coefficients ( $\beta$ ) of the circadian rhythm on day1 and day 2 for each sample. To determine if a subject had a consistent or an inconsistent circadian rhythm, a difference  $\beta$  score was produced by subtracting day 1 coefficient ( $\beta$ ) from day

2 coefficient ( $\beta$ ). The difference  $\beta$  score was then converted to an absolute value. The absolute value was used to categorize the circadian rhythm as consistent or an inconsistent. The consistent rhythm was defined as the absolute difference  $\beta$  value less than one standard deviation of the difference  $\beta$  score, and the inconsistent rhythm was defined as the absolute difference  $\beta$  value greater than one standard deviation of the difference  $\beta$  score. In this study, one standard deviation of the difference  $\beta$  score was 0.563 for raw data, and 0.573 for log transformed data.

Using this procedure, seventeen percent of the participants ( $n = 9$ ) had an inconsistent circadian rhythm and eighty-three percent of the participants ( $n = 44$ ) had a consistent circadian rhythm based on raw salivary cortisol data. For log transformed salivary cortisol data, twenty-one percent of the participants ( $n = 11$ ) had an inconsistent circadian rhythm and seventy-nine percent of the participants ( $n = 42$ ) had a consistent circadian rhythm. Figure 9-1 and 9-2 shows the mean circadian rhythm of the consistent group and inconsistent group on day 1 and day 2 based on raw salivary cortisol data. Figure 10-1 and 10-2 shows the log transformed mean circadian rhythm of the consistent group and inconsistent group on day 1 and day 2.

Figure 9-1.

*Circadian Rhythm of the Consistent Group Based on Raw Data (n=44)*

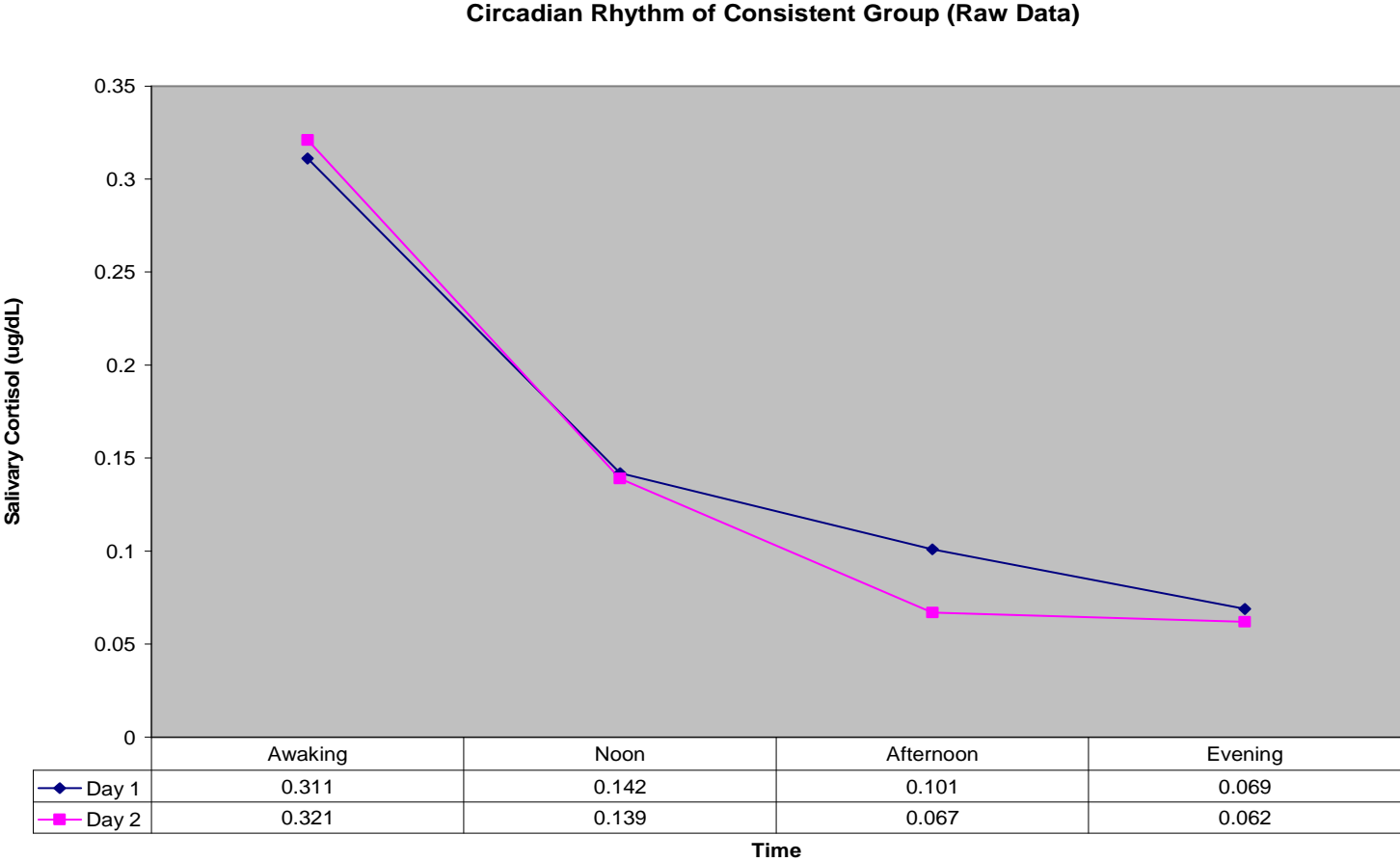


Figure 9-2.  
*Circadian Rhythm of the Inconsistent Group Based on Raw Data (n=9)*

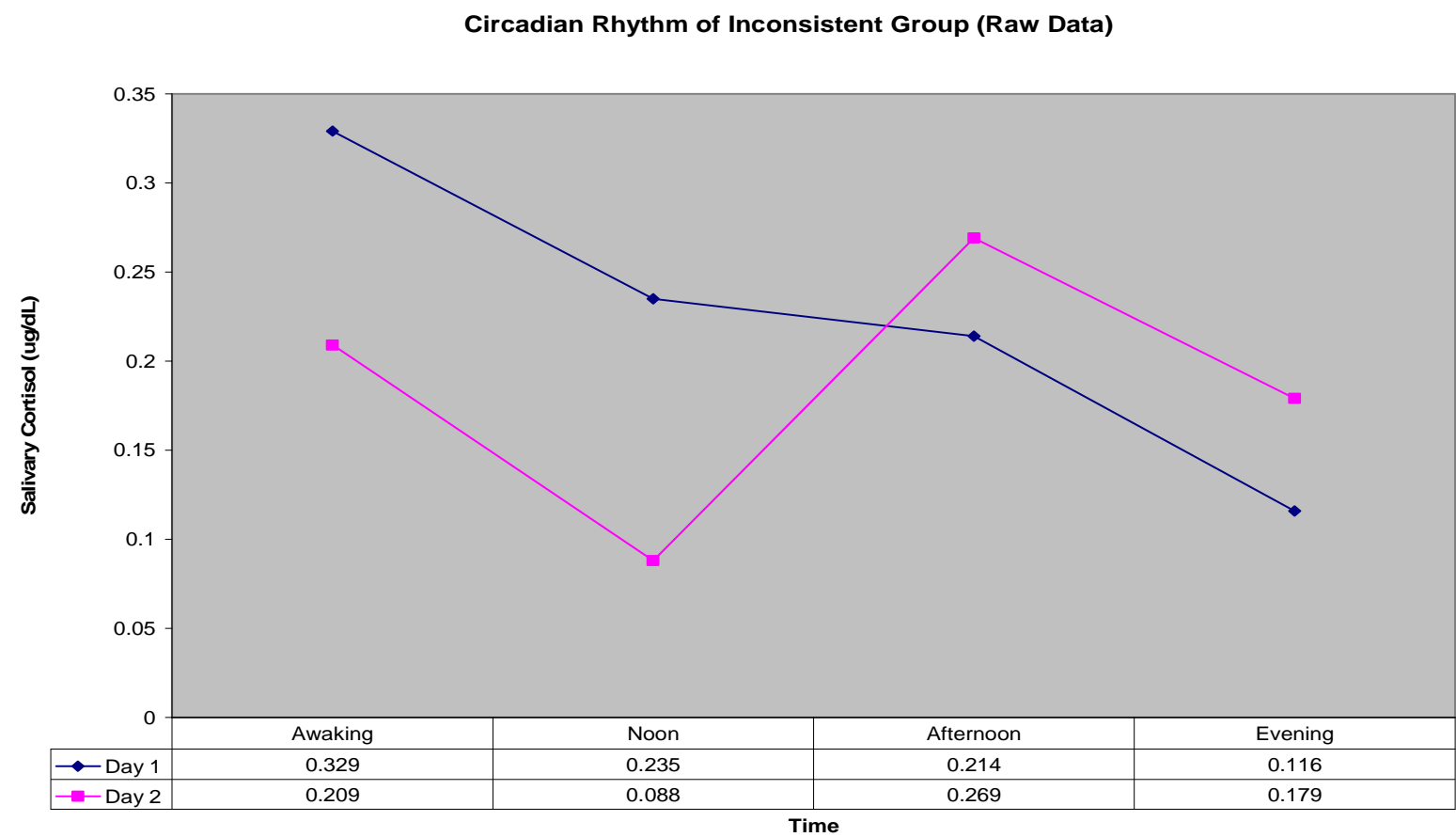


Figure 10-1.

*Circadian Rhythm of the Consistent Group Based on Log Transformed Data (n=42)*

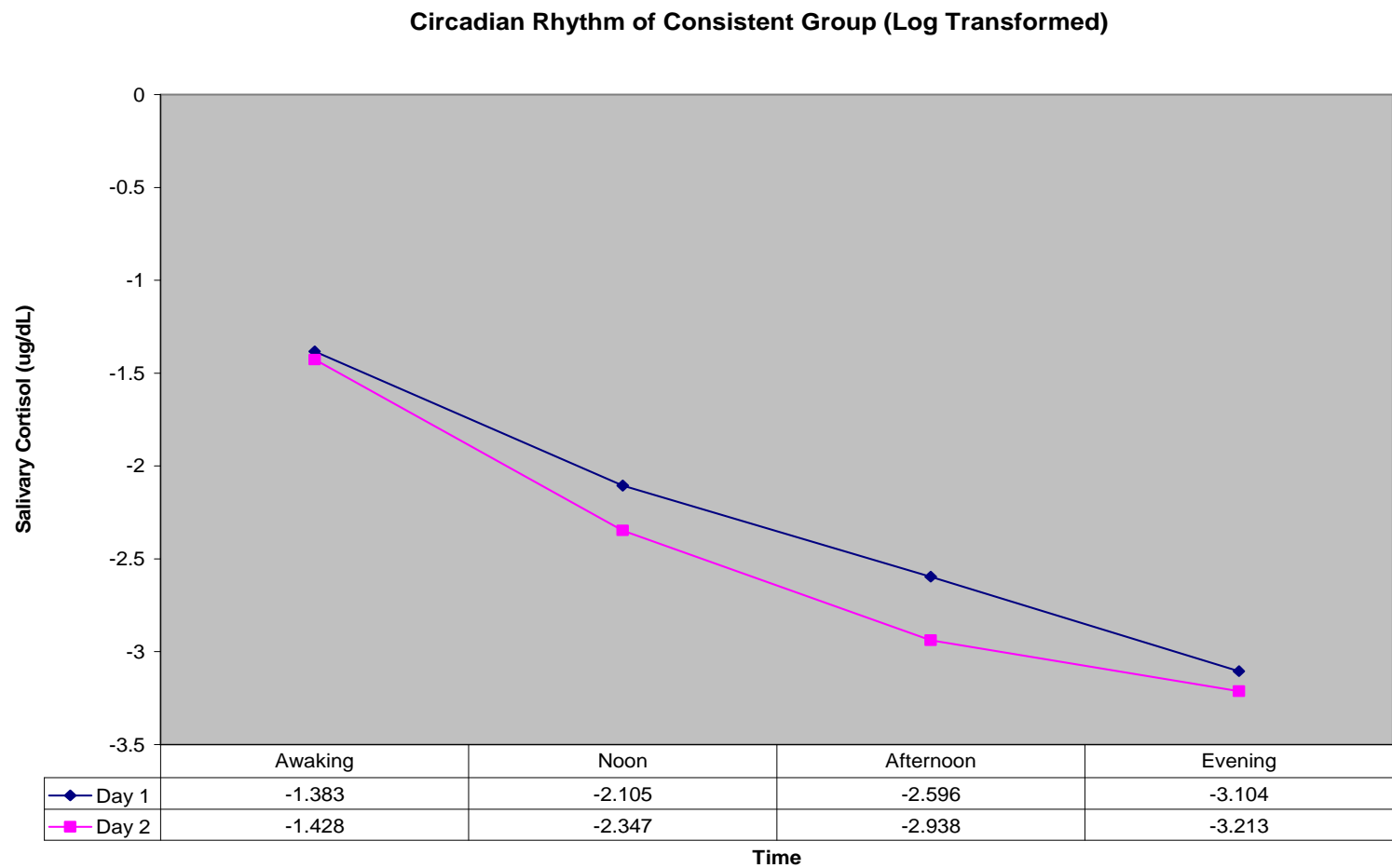
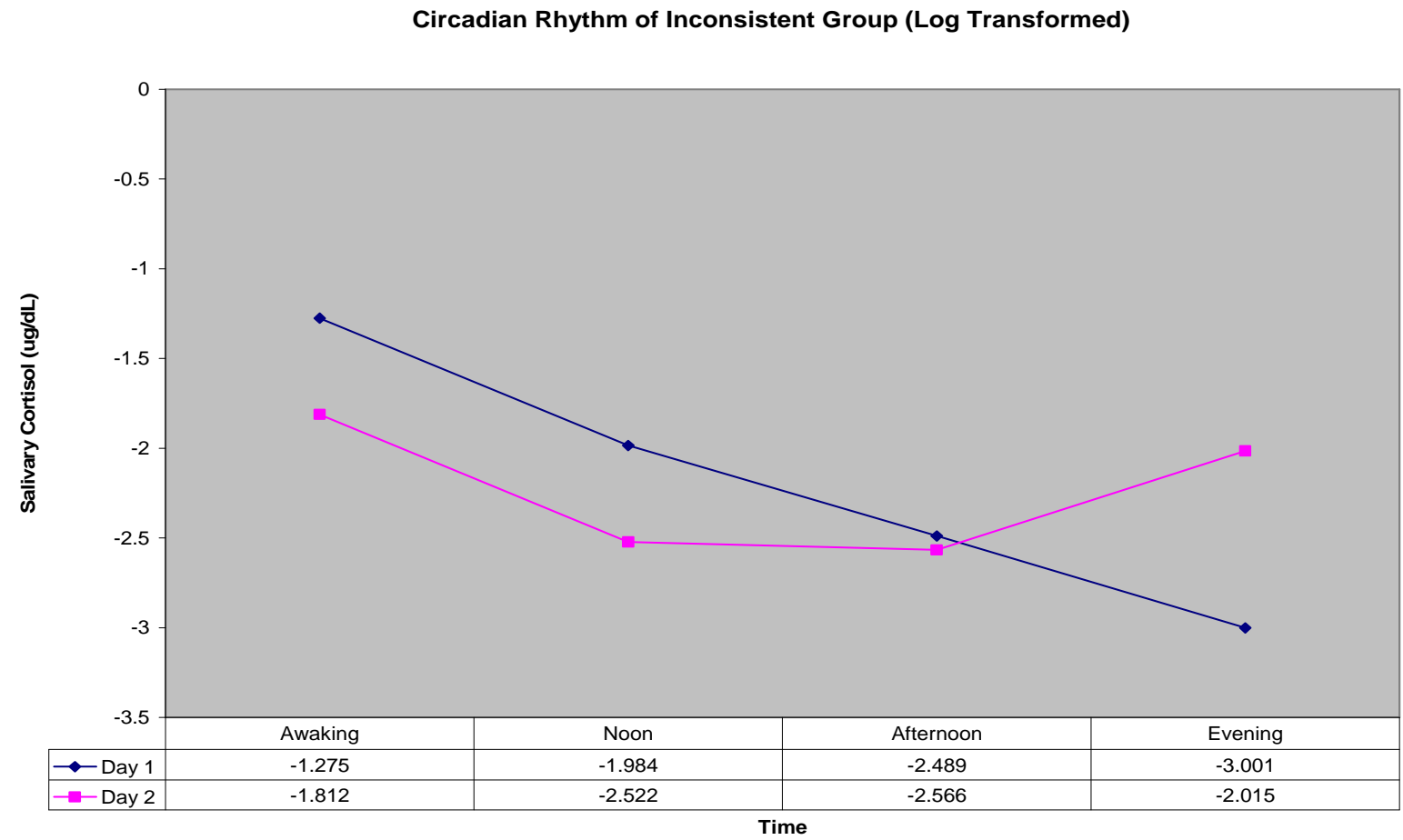


Figure 10-2.

*Circadian Rhythm of the Inconsistent Group Based on Log Transformed Data (n=11)*



*The Consistent Circadian Rhythm Group*

Eighty-three percent of the participants ( $n = 44$ ) had a consistent circadian rhythm based on raw salivary cortisol data. Seventy-nine percent of the participants ( $n = 42$ ) had a consistent circadian rhythm based on log transformed salivary cortisol data. Mean, standard deviation, and range of the difference beta scores are summarized in Table 8. The mean difference beta for the consistent circadian rhythm group was 0.037 ( $SD = 0.225$ ) with a range of -0.555 to 0.535, based on raw salivary cortisol data. The log transformed mean difference beta for the consistent circadian rhythm group was 0.055 ( $SD = 0.242$ ) with a range of -0.438 to 0.511.

Table 8.

*Mean Difference Beta Score between 2 days in Consistent Circadian Rhythm Group*

	Mean	SD	Range
The Difference Beta ( $\beta$ )			
Raw Data ( $n = 44$ )	0.037	0.225	-0.555 - 0.535
Log Transformed Data ( $n = 42$ )	0.055	0.242	-0.438 - 0.511

*The Inconsistent Circadian Rhythm Group*

Seventeen percent of the participants ( $n = 9$ ) had an inconsistent circadian rhythm based on raw salivary cortisol data. Twenty-one percent of the participants ( $n = 11$ ) had an inconsistent circadian rhythm based on log transformed salivary cortisol data. Mean, standard deviation, and range of the difference beta scores are summarized in Table 9. The mean of the difference beta for the inconsistent circadian rhythm group was 0.954 ( $SD = 0.972$ ) with a range of -1.371 to 1.842, based on raw salivary cortisol data. The log transformed mean difference beta for the inconsistent circadian rhythm group was 0.678 ( $SD = 1.061$ ) with a range of -1.239 to 1.830.

Table 9.

*Mean Difference Beta Score between 2 days in Inconsistent Circadian Rhythm Group*

	Mean	SD	Range
The Difference Beta ( $\beta$ )			
Raw Data ( $n=9$ )	0.954	0.972	-1.371 - 1.842
Log Transformed Data ( $n=11$ )	0.678	1.061	-1.239 - 1.830



*The Typical Negative Circadian Rhythm and Non-typical Flat Circadian Rhythm*

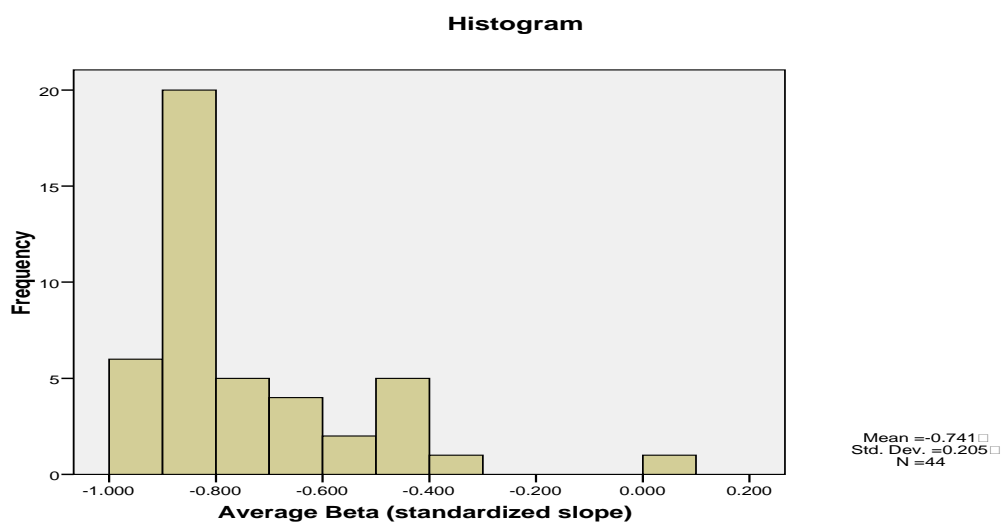
Typical negative or non-typical flat circadian rhythms had been identified within the consistent rhythm group in previous studies (Ice et al., 2004; Smyth et al., 1997). In order to determine if there was a typical negative rhythm or a non typical flat rhythm, the average beta for the individuals with consistent rhythm was calculated and plotted. The distribution of the average beta for the consistent circadian rhythm is shown in Figure 11-1 (raw data) and 11-2 (log transformed data).

In this study, the cut-point for defining the typical negative rhythm and non-typical flat rhythm was set as - 0.05. The value of - 0.05 was a point on the horizontal axis and was between the distributions of typical negative and non-typical flat rhythms. Using the cut-point value of - 0.05, the typical negative circadian rhythm group was apparent as the main distribution of scores and that the one positive outlier could be considered as coming from a distribution of non-typical flat scores. Of the forty-four participants with consistent circadian rhythm, forty-three participants (98 %, average beta < - 0.05) were characterized as having a typical negative circadian rhythm and one participant (2 %, average beta > - 0.05) was characterized as having non-typical flat rhythm, based on raw salivary cortisol data. Of the forty-two participants with consistent circadian rhythm based on log transformed data, forty-one participants (98 %, average beta < - 0.05) were characterized as having a typical negative circadian rhythm, and one participant (2 %, average beta > - 0.05) was characterized as having a non-typical flat rhythm.

The findings revealed that virtually all of the sample in the consistent group had a typical, negative circadian rhythm. See Figure 12-1 and 12-2 (a typical negative circadian rhythm), and Figure 13-1 and 13-2 (a non-typical flat circadian rhythm).

*Figure 11-1.*

Distribution of the Average Beta from Consistent Circadian Rhythm Group (Raw Date)

*Figure 11-2.*

Distribution of the Average Beta from Consistent Circadian Rhythm Group (Log Transformed Data)

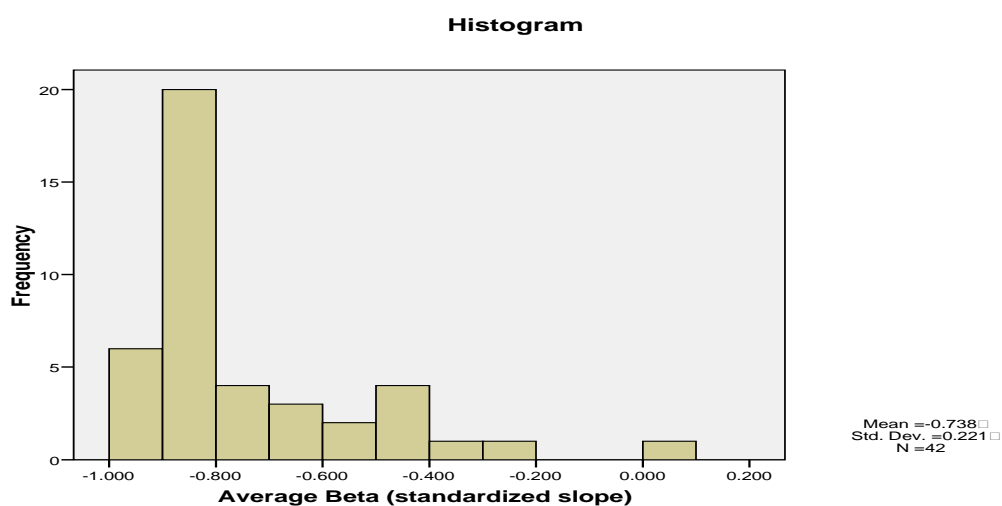


Figure 12-1.

Typical Negative Circadian Rhythm Based on Raw Data (n=43)

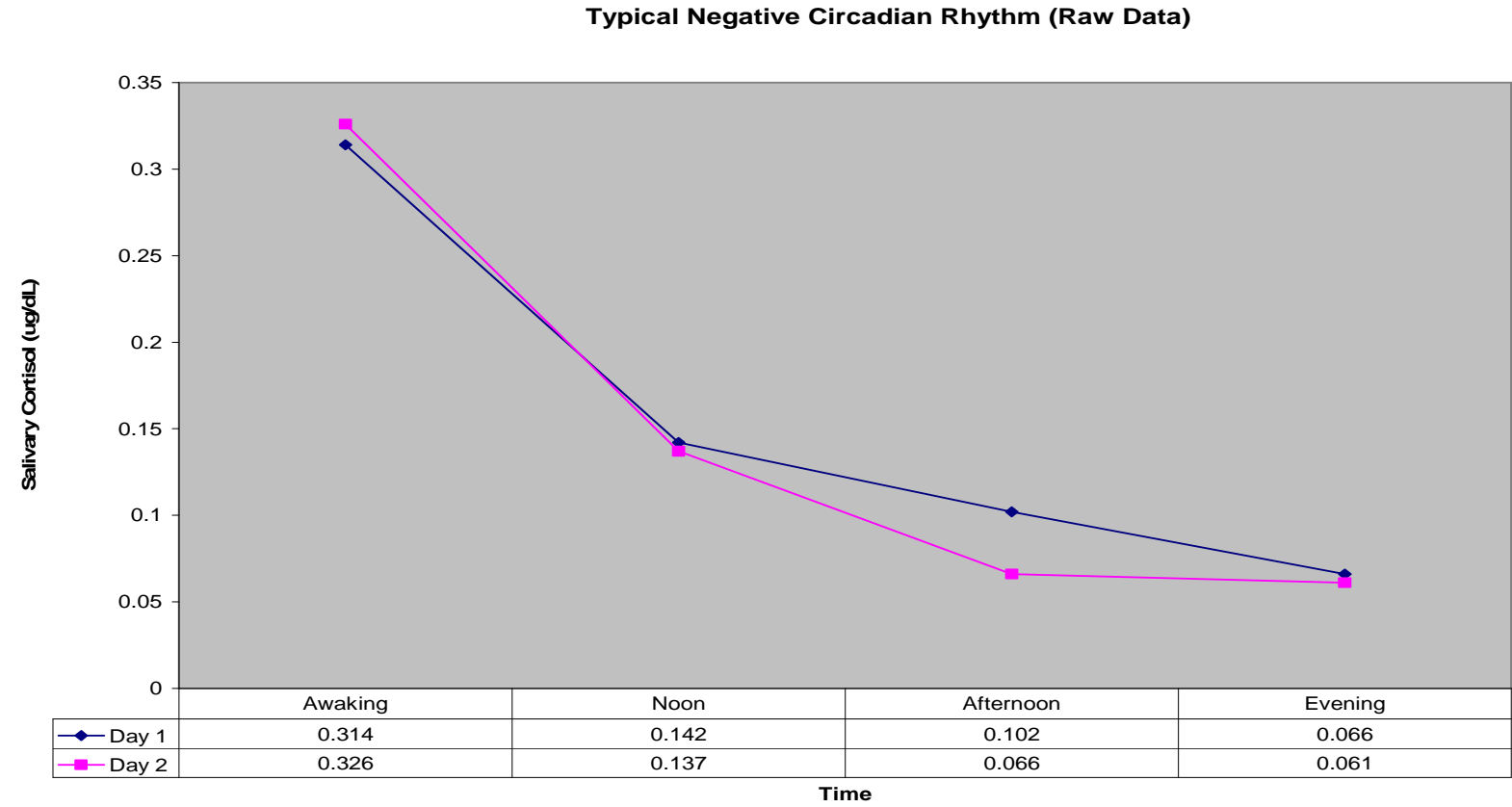


Figure 12-2.

Typical Negative Circadian Rhythm Based on Log Transformed Data (n=41)

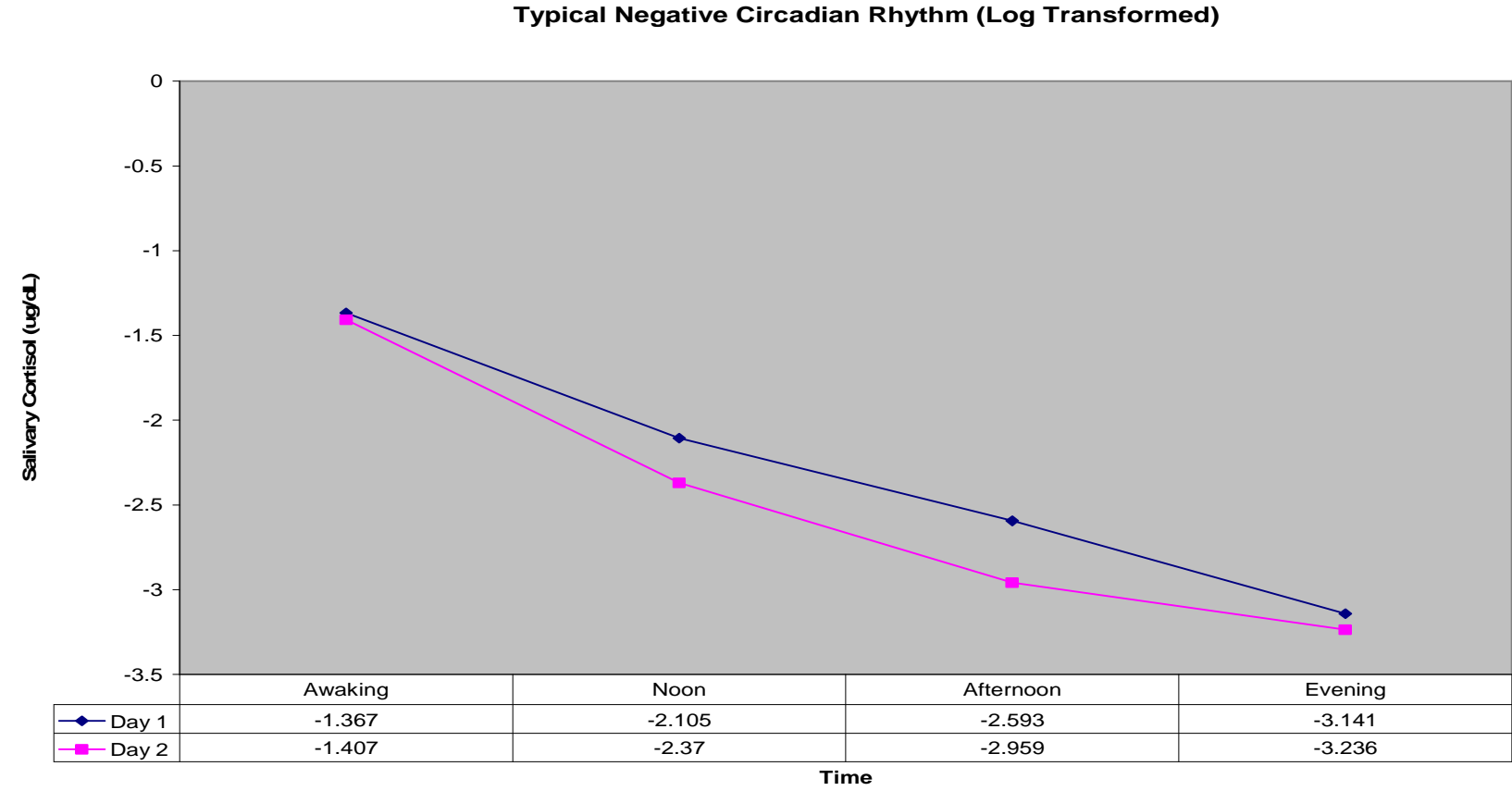


Figure 13-1.

*Non-typical Flat Circadian Rhythm Based on Raw Data (n=1)*

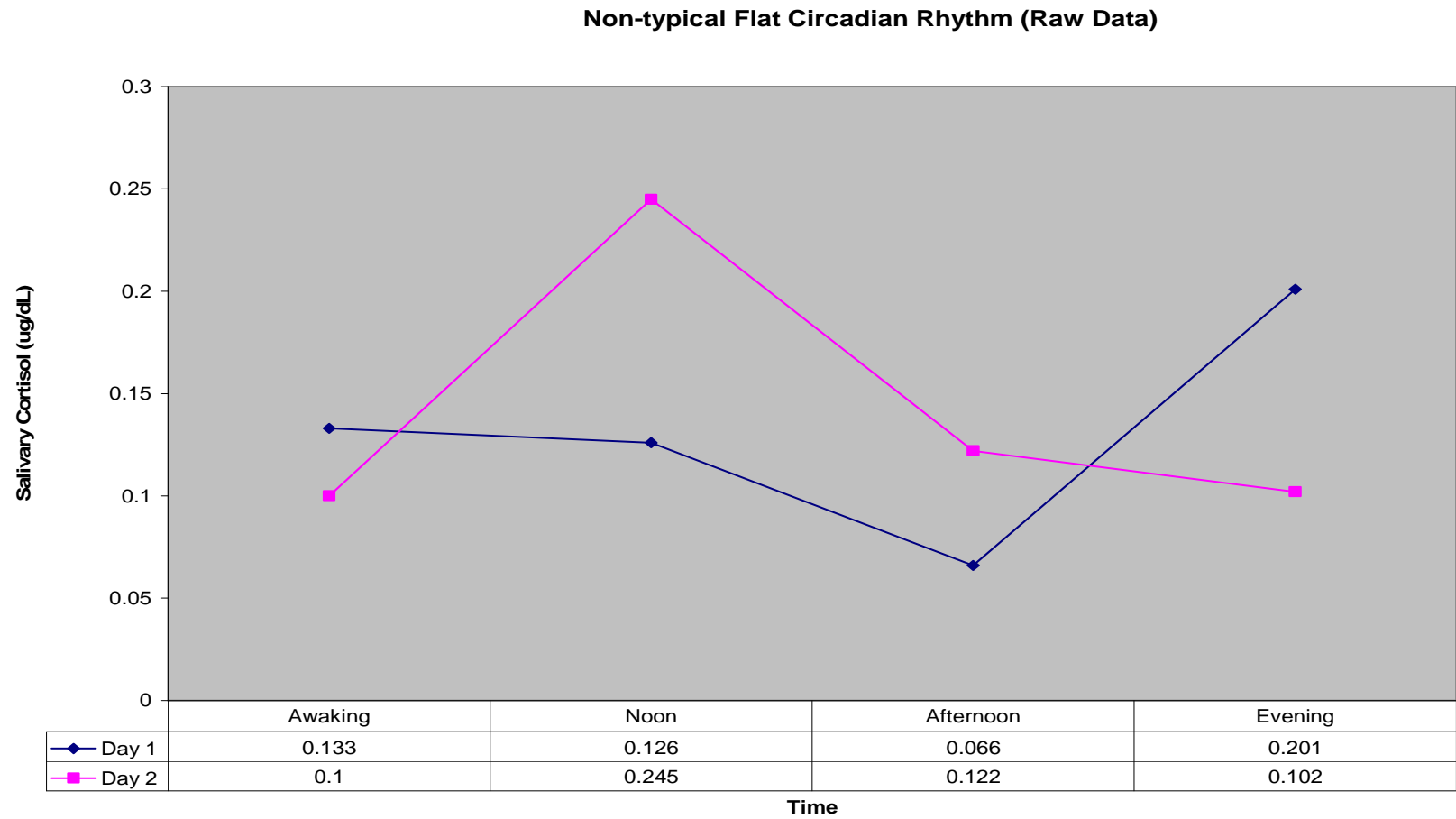
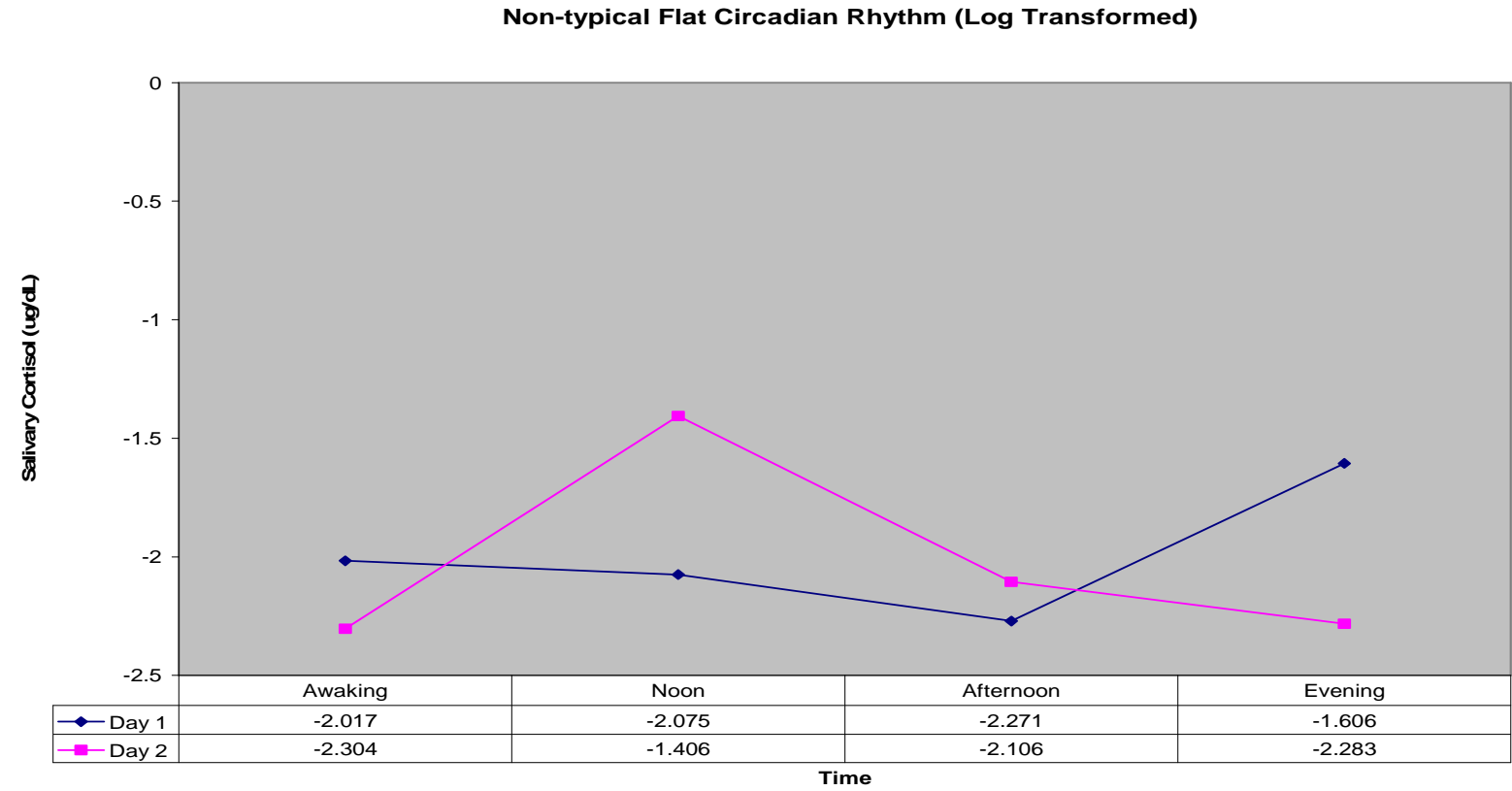


Figure 13-2.

*Non-typical Flat Circadian Rhythm Based on Log Transformed Data (n=1)*



*The Relationships between the Consistency of Circadian Rhythm and Study Variables*

Pearson's correlations were calculated to determine the relationships among salivary cortisol indices (Slope,  $AUC_G$ , and  $AUC_I$ ) and other variables (perceived stress, symptoms, symptom distress, and symptom self-management) in the consistent circadian rhythm group. A Spearman's rho was used to determine these correlations in the inconsistent circadian rhythm group. This nonparametric statistics was used because of the small sample size. The mean  $AUC_G$  salivary cortisol (raw data and log transformed data) was significantly and inversely associated with symptom self-management strategies ( $r = -.929$ ,  $p < .01$  and  $r = -.612$ ,  $p < .05$ , respectively) in the inconsistent circadian rhythm group. See Table 10.

Table 10.

*Spearman's rho Correlations between Salivary Cortisol ( $AUC_G$ ) and Symptom Self-Management Strategies in the Inconsistent Circadian Rhythm Group*

	$AUC_G$ (Raw Data) ( $n=9$ )	$AUC_G$ (Log Transformed Data) ( $n=11$ )
Symptom Self-management Strategies	-.929**	-.612*

\*  $p < .05$ , \*\*  $p < .01$

There were no significant correlations among the salivary cortisol indices (Slope,  $AUC_G$ , and  $AUC_I$ ) and other variables (perceived stress, symptoms, symptom distress, and symptom self-management) in the consistent circadian rhythm group.



*Demographics of the Differences in Circadian Rhythm Consistency*

A series of independent T-test and chi-square analyses were conducted to determine if the differences in circadian rhythm consistency were based on demographic characteristics and study measures (stress, symptoms, symptom distress, and symptom self-management). Table 11 summarizes the differences in demographics and study measures (stress, symptoms, symptom distress, and symptom self-management) in the consistent circadian rhythm group and the inconsistent circadian rhythm group.

In the consistent circadian rhythm group, the mean age of the sample was 67.7 years, and the majority of participants were Caucasian, married and retired. In the inconsistent circadian rhythm group, the mean age was older (69.6 years) than in the consistent group. The majority of participants in the inconsistent group was employed, had higher PSA levels, and reported higher scores on perceived stress, symptoms, symptom distress, and lower scores on symptom self-management strategies. However, the findings revealed that there were no significant differences between the groups on any demographic or study measures.

Table 11.

*Demographics of the Differences in Circadian Rhythm Consistency*

n=53	Consistent Group (n=44)	Inconsistent Group (n=9)
Age in years	67.7 (7.0)	69.6 (6.5)
Ethnic (%)		
Caucasian	37 (70 %)	6 (11 %)
African-American	3 (5 %)	2 (4 %)
Hispanic	4 (8 %)	1 (2 %)
Education	16.1 (3.3)	16.8 (4.3)
Marital status (%)		
Single	2 (4 %)	0 (0 %)
Married	30 (57 %)	8 (15 %)
Divorced	11 (20 %)	1 (2 %)
Widowed	1 (2 %)	0 (0 %)
Income		
Income exceeds my expenses	30 (57 %)	7 (13 %)
Income meets my expenses	12 (23 %)	2 (4 %)
Income barely meets my expenses	2 (4 %)	0 (0 %)
Currently employed		
Yes	16 (30 %)	6 (11 %)
No	28 (53 %)	3 (6 %)
PSA at diagnosis (ng/mL)	6.21 (2.45)	8.03 (5.20)
Time since diagnosis (month)	7.48 (6.20)	4.89 (2.80)
Treatment (%)		
- Prostatectomy	18 (34 %)	6 (11 %)
- Radiation therapy	26 (49 %)	3 (6 %)
Salivary cortisol (ug/dL)		
- AUC <sub>G</sub>	2.074 (.913)	3.064 (1.887)
- AUC <sub>I</sub>	-2.626 ( 2.840)	-.974 (1.746)
- Slope	-.741 (-.204)	-.166 (.162)
Perceived Stress Scale	9.48 (5.72)	9.89 (7.21)
Symptoms	42.95 (8.80)	44.33 (7.87)
Symptom Distress	29.19 (11.42)	31.56 (9.34)
Symptom Self-Management Strategies	36.19 (21.86)	31.00 (18.62)

### Research Question Two

What are the levels of the psychological stress response as measured by the Perceived Stress Scale? Are there any differences in the 2 subgroups?

The psychological stress response was defined as perceived stress and measured by the Perceived Stress Scale (PSS). Mean, standard deviation, and range of perceived stress scores are summarized in Table 12. The mean of the PSS for the total sample was 9.55 (SD = 5.92) with a range of 0~24. The PSS mean scores of the radiation therapy group were (M = 10.07, SD = 6.07) higher than the radical prostatectomy group (M = 8.92, SD = 5.8). However, there was no significant difference between the subgroups on the score of perceived stress ( $t = -.701$ ;  $p < .05$ ).

Table 12.

*Perceived Stress Scores: Total Sample and Subgroups (n=53)*

	Mean	SD	Range
Total samples (n=53)	9.55	5.92	0-24
Radical Prostatectomy (n=24)	8.92	5.80	0-18
Radiation Therapy (n=29)	10.07	6.07	1-24

### Research Question Three

What is the relationship between the physiological stress response and the psychological stress response?

Tables 13-1 and 13-2 summarize the Pearson's correlations between perceived stress and salivary cortisol (raw data and log transformed data). Perceived stress was positively correlated with mean salivary cortisol (raw data) at noon ( $r = .517$ ,  $p < .01$ ),

afternoon ( $r = .398$ ,  $p < .01$ ), and  $AUC_G$  ( $r = .410$ ,  $p < .01$ ). Perceived stress was positively correlated with mean salivary cortisol (log transformed data) at noon ( $r = .487$ ,  $p < .01$ ), and afternoon ( $r = .381$ ,  $p < .01$ ),  $AUC_G$  ( $r = .394$ ,  $p < .01$ ), and  $AUC_I$  ( $r = .280$ ,  $p < .05$ ). There was no statistically significant relationship between perceived stress and mean slope of salivary cortisol (raw data and log transformed).

Table 13-1.

*Bivariate Correlations between Perceived Stress and Salivary Cortisol Variables (Raw Data, n=53)*

	Salivary Cortisol						
	Awaking	Noon	Afternoon	Evening	Slope ( $\beta$ )	$AUC_G$	$AUC_I$
Total Perceived stress	-.025	.517**	.398**	.112	.047	.410**	.205

\*  $p < .05$ , \*\*  $p < .01$

Table 13-2.

*Bivariate Correlations between Perceived Stress and Salivary Cortisol Variables (Log Transformed Data, n=53)*

	Salivary Cortisol						
	Awaking	Noon	Afternoon	Evening	Slope ( $\beta$ )	$AUC_G$	$AUC_I$
Total Perceived stress	.053	.487**	.381**	.071	.007	.394**	.280*

\*  $p < .05$ , \*\*  $p < .01$

## **Aim Two**

To describe the severity and frequency of symptoms and the degree of symptom distress experienced by men with localized prostate cancer following radical prostatectomy or radiation therapy. There were three research questions.

### **Research Question One**

What levels of symptoms (severity and frequency) do men with localized prostate cancer following radical prostatectomy or radiation therapy experience?

### **Research Question Two**

What is the degree of symptom distress among men with localized prostate cancer following radical prostatectomy or radiation therapy?

Findings for research question one and research question two are discussed below. Mean, standard deviation, and range of the Symptom Indexes are summarized in Table 14. The mean of the Symptom Indexes was 72.79 (SD = 17.95) with a range of 45 to 119. The mean of the Symptoms Subscale (urinary, bowel, and sexual functioning) was 43.19 (SD = 8.59) with a range of 28 to 58. Sample mean for the Symptom Related Distress was 29.60 (SD = 11.05) with a range of 15 to 61.

For the Symptoms Subscale, the mean scores were 16.77 (SD = 4.31) for urinary problems, 8.83 (SD = 3.43) for bowel problems, and 17.58 (SD = 5.49) for sexual functioning. For the Symptom Related Distress Subscale, the mean scores were 10.34 (SD = 3.97) for urinary symptom distress, 5.60 (SD = 2.38) for bowel symptom distress, and 13.67 (SD = 7.59) for sexual functioning distress. Refer to Table 14.

Table 14.

*Description of the Symptom Indexes Scores for Total Sample (n=53)*

	Mean	SD	Range
Symptom Indexes	72.79	17.95	45-119
Symptoms	43.19	8.59	28-58
Urinary Problems	16.77	4.31	10-29
Bowel Problems	8.83	3.43	6-20
Sexual Functioning	17.58	5.49	9-23
Symptom Related Distress	29.60	11.05	15-61
Urinary Symptoms Distress	10.34	3.97	6-22
Bowel Symptoms Distress	5.60	2.38	4-14
Sexual Functioning Distress	13.67	7.59	5-25

Table 15 summarizes the descriptive statistics of the Symptom Index (Symptoms subscale and Symptom Related Distress subscale) for the radiation therapy and prostatectomy groups. The mean scores of the Symptom Indexes were 77.29 (SD = 17.47) for the radical prostatectomy group and 68.92 (SD = 17.73) for the radiation group. The mean scores of the Symptoms were 45.58 (SD = 8.06) for the radical prostatectomy group and 41.14 (SD = 8.673) for the radiation group. The mean scores of the Symptom Related Distress were 31.70 (SD = 11.59) for the radical prostatectomy group and 27.78 (SD = 10.41) for the radiation group. However, there were no statistically significant differences in the scores on the Symptom Indexes, Symptoms subscale, and Symptom Related Distress subscale between the prostatectomy group and the radiation therapy group.

The prostatectomy group reported higher mean scores on urinary symptoms (M = 18.66, SD = 4.31) and sexual functioning symptoms (M = 19.50, SD = 5.25) than did the radiation

therapy group. The radiation therapy group had a higher mean score on bowel symptoms ( $M = 10.01$ ,  $SD = 3.88$ ). There were significant differences between the prostatectomy group and radiation therapy group on urinary symptoms ( $t = 3.150$ ,  $p < .01$ ), sexual functioning symptoms ( $t = 2.448$ ,  $p < .05$ ), and bowel symptoms ( $t = -3.017$ ,  $p < .01$ ).

On the Symptom Related Distress subscale, the prostatectomy group reported higher scores on urinary symptom distress ( $M = 10.83$ ,  $SD = 4.22$ ) and sexual dysfunction distress ( $M = 15.92$ ,  $SD = 7.59$ ) than did the radiation therapy group. The radiation therapy group reported a higher mean score of bowel symptom distress ( $M = 6.14$ ,  $SD = 2.50$ ). However, there was a significant difference across subgroups in sexual dysfunction distress, but no significant differences in urinary symptom distress and bowel symptom distress.



Table 15.

*Symptom Indexes Scores by Subgroups (n=53)*

	Radical Prostatectomy (n=24)	Radiation Therapy (n=29)	<i>t</i>	<i>p</i>
	<i>Mean (SD)</i>	<i>Mean (SD)</i>		
Symptom Index	77.29 (17.47)	68.92 (17.73)	1.706	.94
Symptoms	45.58 (8.06)	41.14 (8.63)	1.905	.63
Urinary Problems	18.66 (4.31)	15.20 (3.68)	3.150	.003
Bowel Problems	7.41 (2.12)	10.01 (3.88)	-3.071	.004
Sexual Functioning	19.50 (5.25)	15.92 (5.24)	2.448	.018
Symptom Related Distress	31.70 (11.59)	27.78 (10.41)	1.285	.205
Urinary Symptom Distress	10.83 (4.22)	9.93 (3.76)	.822	.415
Bowel Symptom Distress	4.96 (2.10)	6.14 (2.50)	-1.836	.072
Sexual Functioning Distress	15.92 (7.59)	11.75 (7.00)	2.057	.045

### Research Question Three

What is the relationship between symptoms and symptom distress among men with localized prostate cancer following radical prostatectomy or radiation therapy?

A Pearson correlation was computed to examine the strength and direction of the relationship between symptoms and symptom distress. Table 16 summarizes the correlations between symptoms and symptom distress. The Symptoms (urinary problems, bowel problems, and sexual functioning) were positively correlated with Symptom Related Distress (urinary symptom distress, bowel symptom distress, and sexual dysfunction distress) ( $r = .665$ ,  $p < .01$ ). Greater symptom severity and frequency were associated with greater symptom related distress among men who either were treated with prostatectomy or radiation therapy.

Urinary symptoms positively correlated with urinary symptom distress ( $r = .732$ ,  $p < .01$ ) and sexual dysfunction symptom distress ( $r = .426$ ,  $p < .01$ ). Greater symptoms of urinary problems (urinary incontinence, urinary obstruction/irritation) were associated with greater sexual dysfunction distress. Bowel symptoms positively correlated with bowel symptom distress ( $r = .808$ ,  $p < .01$ ), urinary symptom distress ( $r = .321$ ,  $p < .05$ ), and sexual dysfunction distress ( $r = .275$ ,  $p < .05$ ). Greater bowel symptoms were associated with greater bowel symptom distress, urinary symptom distress, and sexual dysfunction distress. Sexual functioning symptoms positively correlated with sexual dysfunction distress ( $r = .311$ ,  $p < .05$ ). Greater symptoms of sexual functioning were associated with greater sexual dysfunction distress in men with prostate cancer who underwent prostatectomy or radiation therapy.

Table 16.

*Bivariate Correlations between Symptoms and Symptom Related Distress*

<u>Symptom Related distress</u>		Urinary Distress (n=53)	Bowel Distress (n=53)	Sexual Distress (n=52)	<u>Symptoms</u>		
					Urinary Problems (n=53)	Bowel Problems (n=53)	Sexual Functioning (n=52)
<u>Symptoms</u>	.665**	.521**	.471**	.588**			
- Urinary Problems		.732**	.192	.426**		.074	.084
- Bowel Problems		.321*	.808**	.275*	.074		.155
- Sexual Functioning		.079	.116	.375**	.084	.155	
<u>Symptom Related distress</u>					.665**		
- Urinary Distress			.538**	.388**	.732**	.321*	.079
- Bowel Distress		.538**		.238	.192	.808**	.116
- Sexual Dysfunction Distress		.388**	.238		.426**	.275*	.375**

\* p &lt; .05, \*\* p &lt; .01

### **Aim Three**

To describe symptom self-management strategies and their perceived effectiveness among men with localized prostate cancer following radical prostatectomy or radiation therapy. There were three research questions.

#### **Research Question One**

What is the frequency of strategies for symptom self-management used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

#### **Research Question Two**

What is the perceived effectiveness of each strategy used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

Findings for questions one and question two are discussed below. Table 17 summarizes the frequency and percentage of the strategies and their effectiveness for each problem. The three domains of symptoms dysfunction for symptom self-management are urinary problems, bowel problems, and sexual dysfunction.

#### *Urinary Symptom Self-Management*

There are six symptoms of urinary dysfunction in urinary symptom self-management. The six urinary problems included leaking urine, slow or difficult urine flow, urinating at night, frequent urination, burning or pain during urination, and urgency in urination. The three most frequently used strategies to alleviate leaking urine were: use pad or adult diaper (45 %), kegel exercise (43 %), and endure or tolerate (30 %). The three highest perceived strategies for effective symptom self-management to alleviate leaking urine were: use of pad or adult diaper (62 %), do kegel exercises (62 %), and

endure/tolerate (43 %). The three most frequently used symptom self-management strategies to alleviate slow or difficult urine flow were: endure/tolerate (40 %), take medicines (21 %), and kegel exercises (7 %). The three highest perceived effective strategies to alleviate leaking urine were: endure/tolerate (54 %), take medicines (321 %), and do kegel exercises (8 %). The three most frequently used strategies for symptom self-management to alleviate urinating at night were: avoiding drinking water before going to bed (62 %), enduring/tolerating (49 %), and using pad or adult diaper (38 %). The three highest perceived effective strategies for urinating at night were: avoiding drinking water before going to bed (60 %), enduring/tolerating (55 %), and using pad or adult diaper (43 %).

To alleviate frequent urination, the three most frequently used symptom self-management strategies were: endure/tolerate (47%), kegel exercises (45 %), and use pad or adult diaper (43 %). The three highest perceived effective strategies for frequent urination were: kegel exercises (54 %), endure/tolerate (51 %), and use pad or adult diaper (49 %). The most frequently used strategies to alleviate burning or pain during urination were endure/tolerate (25 %) and rest (11 %). The highest perceived strategies for effective symptom self-management for burning or pain during urination were endure/tolerate (55 %) and rest (23 %). The three most frequently used strategies of symptom self-management for urgency in urination included endure/tolerate (40 %), take fewer trips (22 %), use pad or adult diaper (22 %), and decrease social activities (18 %). The three highest perceived effective strategies to alleviate urgency in urination were endure/tolerate (54 %), use pad or adult diaper (40 %), and take fewer trips (33 %).

### *Bowel Symptom Self-Management*

There are four symptoms of bowel dysfunction in bowel symptom self-management. The four bowel problems included diarrhea, loose or watery stools, urgency in moving bowels, tenderness or pain, and an urge to move bowels with nothing to pass. The most frequently used symptom self-management strategies to alleviate diarrhea or watery stools included endure/tolerate (36 %), rest (26 %), eat fruit (26 %), drink more water (24 %), eat small portions of food (24 %), avoid fried foods or high fiber foods (19 %), and take medicines (19 %). The highest perceived effective strategies to alleviate diarrhea or watery stools were: endure/tolerate (73 %), rest (53 %), eat fruits (53 %), drink more water (46 %), eat small portions of food (46 %), avoid fried foods (38 %), and take medicines (38 %).

To alleviate urgency in moving the bowels, the most frequently used symptom self-management strategies were take fewer long trips (13 %) and decrease social activities (9 %). The highest perceived effective strategies for urgency in moving the bowels were decrease social activities (46 %) and take fewer trips (40 %). The three most frequently used symptom self-management strategies to alleviate tenderness or pain included endure/tolerate (23 %), rest (15 %), not eat (13 %), and take medicines (13 %). The three highest perceived effectiveness of strategies to alleviate tenderness or pain were endure/tolerate (45 %), rest (40 %), not eat (35 %), and take medicines (35 %). The most frequently used symptom self-management strategies to alleviate an urge to move the bowels with nothing to pass were to take fewer long trips (13 %) and decrease social activities (9 %). Also, taking fewer long trips (46 %) and decreasing social activities (40

%) were the highest perceived effective to alleviate an urge to move the bowels with nothing to pass.

### *Sexual Dysfunction Symptom Self-Management*

The symptom self-management strategies to alleviate sexual dysfunction symptoms included: 1. express feelings with partner, 2. express decreased sexual desire with partner, 3. decrease frequency of sexual activities, 4. find alternative ways (hug, kiss, touch) to express affection, 5. use alternative ways (hug, kiss, touch) to express sexual intimacy, 6. use alternative ways (hug, kiss, touch) to bring each other to orgasm, 7. take medicines, 8. consult therapist or sexual professional, 9. other strategies such as masturbation, and 10. endure/tolerate. The three most frequently used strategies were: express feelings with partner (66%), find alternative ways to express affection (62%), and decrease frequency of sexual activities (59%). The three highest perceived effectiveness of symptom self-management strategies were: express feelings with partner (66%), find alternative ways to express affection (60%), and find alternative ways to express sexual intimacy (55%).

Table 17.

*Symptom Self-Management Strategies and Effectiveness*

	<u>Strategies</u>		<u>Effectiveness</u>	
	Frequency	Percentage	Frequency	Percentage
<b>Urinary Problems</b>				
<b><i>Leaking urine</i></b>	<b>(n=53)</b>		<b>(n=37)</b>	
1. Use pad or adult diaper	24	45 %	23	62 %
2. Take medicines	13	24 %	13	35 %
3. Decrease social activities	14	26 %	12	32 %
4. Fewer long trips	15	28 %	12	32 %
5. Endure/Tolerate	16	30 %	16	43 %
6. Other strategies-Exercise (Kegel)	23	43 %	23	62 %
<b><i>Slow or difficult urine flow</i></b>	<b>(n=53)</b>		<b>(n=34)</b>	
1. Take medicines	11	21 %	11	32 %
2. Endure/Tolerate	21	40 %	20	54 %
3. Other strategies-Exercise (Kegel)	4	7 %	3	8 %
4. Other strategies-Sit on toilet	2	4 %	2	6 %
<b><i>Urinating at night</i></b>	<b>(n=53)</b>		<b>(n=47)</b>	
1. Use pad or adult diaper	20	38 %	20	43 %
2. Avoid drinking water before going to bed	33	62 %	29	60 %
3. Take medicines	14	26 %	13	27 %
4. Endure/Tolerate	26	49 %	26	55 %
5. Other strategies-Sleep with bottle between legs	7	13 %	5	10 %



Table 17. (Continued)

*Symptom Self-Management Strategies and Effectiveness*

	<u>Strategies</u>		<u>Effectiveness</u>	
	Frequency	Percentage	Frequency	Percentage
<b><i>Frequent urination</i></b>	<b>(n=53)</b>		<b>(n=41)</b>	
1. Use pad or adult diaper	23	43 %	20	49 %
2. Take medicines	19	35 %	19	47 %
3. Decreased social activities	20	37 %	14	34 %
4. Fewer long trips	20	37 %	14	34 %
5. Endure/Tolerate	25	47 %	21	51 %
6. Other strategies-Exercise (Kegel)	24	45 %	22	54 %
<b><i>Pain or burning during urination</i></b>	<b>(n=53)</b>		<b>(n=22)</b>	
1. Take medicines	2	4 %	2	9 %
2. Rest	6	11 %	5	23 %
3. Endure/Tolerate	13	25 %	12	55 %
<b><i>Urgency in urination</i></b>	<b>(n=53)</b>		<b>(n=30)</b>	
1. Use pad or adult diaper	12	22 %	12	40 %
2. Take medicines	7	13 %	7	23 %
3. Decreased social activities	10	18 %	10	33 %
4. Fewer long trips	12	22 %	10	33 %
5. Endure/Tolerate	21	40 %	16	54 %
6. Other strategies-Exercise (Kegel)	4	7 %	4	13 %

Table 17. (Continued)

*Symptom Self-Management Strategies and Effectiveness*

	<u>Strategies</u>		<u>Effectiveness</u>	
	Frequency	Percentage	Frequency	Percentage
<b>Bowel Problems</b>				
<i>Diarrhea or loose, watery stools</i>	<i>(n=53)</i>		<i>(n=26)</i>	
1. Try a clear liquid diet	4	7 %	2	7 %
2. Avoid fried foods	10	19 %	10	38 %
3. Avoid high fiber foods	10	19 %	7	27 %
4. Eat frequent, small meals	8	15 %	8	31 %
5. Do things to shift attention (away from problem)	5	9 %	5	19 %
6. Drink more water	13	24 %	12	46 %
7. Eat fruits	14	26 %	14	53 %
8. Eat small portions of food	13	24 %	12	46 %
9. Endure/Tolerate	19	36 %	19	73 %
10. Rest	14	26 %	14	53 %
11. Take medicines	10	19 %	10	38 %
<i>Urgency in moving your bowels</i>	<i>(n=53)</i>		<i>(n=15)</i>	
1. Use pad/adult diaper	2	4 %	1	6 %
2. Decreased social activities	5	9 %	6	40 %
3. Fewer long trips	7	13 %	7	46 %
4. Other strategies-Just go	1	2 %	1	6 %

Table 17. (Continued)

*Symptom Self-Management Strategies and Effectiveness*

	<u>Strategies</u>		<u>Effectiveness</u>	
	Frequency	Percentage	Frequency	Percentage
<b><i>Tenderness or pain</i></b>	<b><i>(n=53)</i></b>		<b><i>(n=20)</i></b>	
1. Endure/Tolerate	12	23 %	9	45 %
2. Do things to shift attention (away from pain)	6	11 %	6	30 %
3. Not eat	7	13 %	7	35 %
4. Massage	4	7 %	3	15 %
5. Rest	8	15 %	8	40 %
6. Take medicines	7	13 %	7	35 %
7. Other strategies-Eat fibers	1	2 %	1	6 %
<b><i>An urge to move bowels with nothing to pass</i></b>	<b><i>(n=53)</i></b>		<b><i>(n=9)</i></b>	
1. Use pad / adult diaper	0	0 %	0	0 %
2. Decreased social activities	3	6 %	4	44 %
3. Fewer long trips	4	7 %	4	44 %
4. Other strategies-Just go	1	2 %	1	11 %

Table 17. (Continued)

*Symptom Self-Management Strategies and Effectiveness*

	<u>Strategies</u>		<u>Effectiveness</u>	
	Frequency	Percentage	Frequency	Percentage
<b>Sexual Functioning</b>	<b>(n=52)</b>		<b>(n=46)</b>	
1. Express feelings with partner	35	66 %	35	66 %
2. Express decreased sexual desire with partner	27	51 %	26	49 %
3. Decrease frequency of sexual activity	31	59 %	26	49 %
4. Find alternative ways to express affection	33	62 %	32	60 %
5. Use alternative ways to express sexual intimacy	29	55 %	29	55 %
6. Use alternative ways to bring each to orgasm	23	43 %	22	41 %
7. Take medicines	9	17 %	5	9 %
8. Consult therapist or sexual professional	0	0 %	0	0 %
9. Other strategies-Masturbation	15	28 %	14	26 %
10. Other strategies-Endure	1	2 %	1	2 %

### **Research Question Three**

What is the relationship between the frequency of using a strategy to alleviate symptoms and the perceived effectiveness of each strategy used by men with localized prostate cancer following radical prostatectomy or radiation therapy?

A Pearson correlation was computed to examine the strength and direction of the relationship between the frequency of using a strategy to alleviate symptoms (urinary problems, bowel problems, and sexual dysfunction) and the perceived effectiveness of each strategy used. Table 18 summarizes the correlations between symptom self-management strategies and symptom self-management effectiveness. The urinary strategies positively correlated with urinary perceived effectiveness ( $r = .626$  to  $.783$ ,  $p < .01$ ). The bowel strategies positively correlated with bowel perceived effectiveness ( $r = .524$  to  $.864$ ,  $p < .01$ ). The sexual functioning strategies positively correlated with sexual functioning perceived effectiveness ( $r = .852$ ,  $p < .01$ ). The finding shows that the more frequently subjects used a strategy to alleviate symptoms the higher its perceived effectiveness. See Table 18.

Table 18.

*Bivariate Correlations between Symptom Self-Management Strategies and Symptom Self-Management Effectiveness*

	<u>Symptom Self-management Strategies: Urinary strategies (n=53)</u>					
	<i>Leaking urine</i>	<i>Slow urine flow</i>	<i>Urinating at night</i>	<i>Frequent urination</i>	<i>Pain</i>	<i>Urgency</i>
<u>Symptom Self-management Effectiveness:</u>						
<u>Urinary Effectiveness</u>						
<i>Leaking urine (n=37)</i>	.783**					
<i>Slow or difficult urine flow (n=34)</i>		.710**				
<i>Urinating at night (n=47)</i>			.714**			
<i>Frequent urination (n=41)</i>				.682**		
<i>Pain or burning during urination (n=22)</i>					.626**	
<i>Urgency in urination (n=30)</i>						.718**

\*\*  $p < .01$

Table 18. (Continued)

*Bivariate Correlations between Symptom Self-Management Strategy and Symptom Self-Management Effectiveness*

<u>Symptom Self-management Strategies: Bowel Strategies (n=53)</u>				
	<i>Diarrhea</i>	<i>Urgency</i>	<i>Tenderness</i>	<i>Urge bowel movement</i>
<u>Symptom Self-management Effectiveness:</u>				
<u><i>Bowel Problems</i></u>				
<i>Diarrhea or loose, watery stools (n=26)</i>	.693**			
<i>Urgency in moving your bowels (n=15)</i>		.524**		
<i>Tenderness or pain (n=20)</i>			.791**	
<i>An urge to move bowels with nothing to pass (n=9)</i>				.864**
<u>Symptom Self-management Strategies:</u>				
<u><i>Sexual Functioning Strategies (n=53)</i></u>				
<u>Symptom Self-management Effectiveness:</u>				
<i>Sexual Functioning (n=46)</i>			.852**	

\*\*  $p < .01$

### **Aim Four**

To examine the relationships among stress (physiological and psychological responses), symptoms, symptom distress, and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy. There were five research questions.

#### **Research Question One**

What are the relationships among stress, symptoms, symptom distress, and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy?

A Pearson correlation was computed to examine the strength and direction of the relationships among stress, symptoms, symptom distress, and symptom self-management. Table 19-1 summarizes the Pearson's correlations among salivary cortisol (raw data), perceived stress, symptoms, symptom distress, and symptom self-management. The mean slope of salivary cortisol positively correlated with  $AUC_G$  salivary cortisol ( $r = .323$ ,  $p < .05$ ) and  $AUC_I$  salivary cortisol ( $r = .397$ ,  $p < .01$ ). The mean  $AUC_G$  salivary cortisol positively correlated with perceived stress ( $r = .410$ ,  $p < .01$ ). Perceived stress positively correlated with symptom distress ( $r = .339$ ,  $p < .05$ ). The total symptoms score (severity and frequency) was significantly and positively correlated with the total score for symptom distress ( $r = .665$ ,  $p < .01$ ), and symptom self-management strategy ( $r = .478$ ,  $p < .01$ ). The total symptom related distress score was positively correlated with symptom self-management strategies ( $r = .561$ ,  $p < .01$ ). There were no statistically



significant correlations among mean slope of salivary cortisol, perceived stress, symptoms, symptom distress, and symptom self-management strategies.

Table 19-1.

*Bivariate Correlations among Stress, Symptoms and Symptom Distress, and Symptom Self-Management (Raw Data)*

	Stress ( <i>n</i> =53)			Perceived Stress	Symptom Indexes ( <i>n</i> =52)		Symptom Self-Management ( <i>n</i> =53)
	Salivary Cortisol				Symptoms	Symptom Related Distress	The Frequency of Strategies
	<i>Slope</i> (β)	<i>AUC<sub>G</sub></i>	<i>AUC<sub>I</sub></i>				
<i>Salivary cortisol</i>							
<i>Slope</i> (β)		.323*	.397**	.047	.089	.133	.032
<i>AUC<sub>G</sub></i>	.323		-.217	.410**	-.020	.087	-.257
<i>AUC<sub>I</sub></i>	.397**	-.217		.205	.084	.150	.167
Perceived Stress	.047	.410**	.205		.183	.339*	.131
Symptoms	.089	-.020	.084	.183		.665**	.478**
Symptom Related Distress	.133	.087	.150	.339*	.665**		.561**
Frequency of Strategies	.032	-.257	.167	.131	.478**	.561**	

\*  $p < .05$ , \*\*  $p < .01$

Correlations among salivary cortisol (log transformed data), perceived stress, symptoms, symptom distress, and symptom self-management are summarized in Table 19-2. The mean slope of salivary cortisol positively correlated with  $AUC_G$  ( $r = .400$ ,  $p < .01$ ) and  $AUC_I$  ( $r = .596$ ,  $p < .01$ ). The mean  $AUC_G$  salivary cortisol positively correlated with  $AUC_I$  ( $r = .426$ ,  $p < .01$ ) and perceived stress ( $r = .394$ ,  $p < .01$ ). The mean  $AUC_I$  salivary cortisol positively correlated with  $AUC_G$  ( $r = .596$ ,  $p < .01$ ), perceived stress ( $r = .280$ ,  $p < .05$ ), and symptom distress ( $r = .318$ ,  $p < .05$ ). There were no statistically significant correlations among mean slope of salivary cortisol (log transformed), perceived stress, symptoms, symptom distress, and symptom self-management strategies.

Figure 14 depicts the significant correlations among stress, symptoms, symptom distress, and symptom self-management.

Table 19-2.

*Bivariate Correlations among Stress, Symptoms and Symptom Distress, and Symptom Self-Management (Log Transformed Data)*

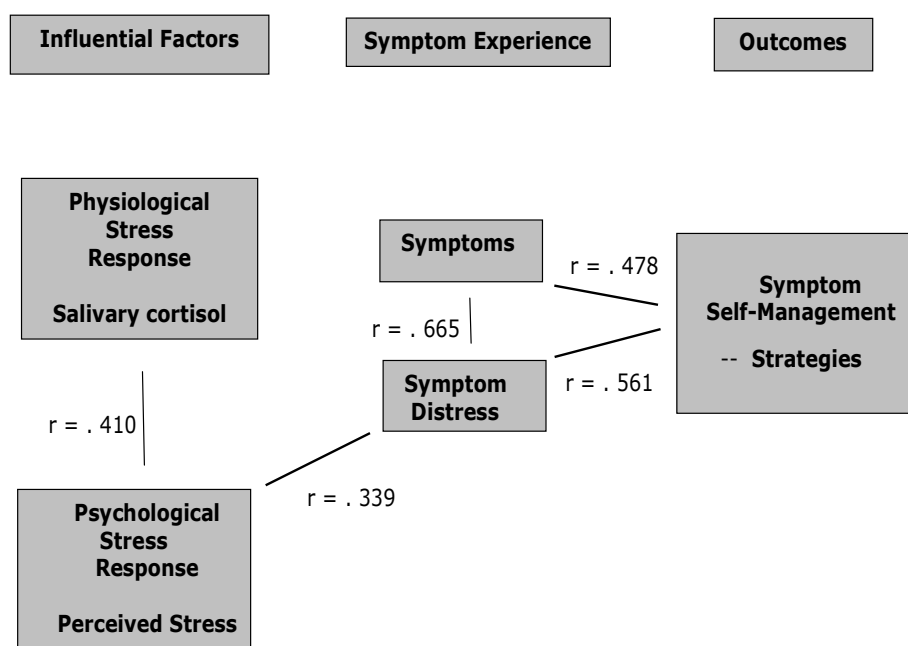
	Stress ( <i>n</i> =53)			Perceived Stress	Symptom Indexes ( <i>n</i> =52)		Symptom Self-Management ( <i>n</i> =53)
	Salivary Cortisol				Symptoms	Symptom Related Distress	The Frequency of Strategies
	<i>Slope</i> (β)	<i>AUC<sub>G</sub></i>	<i>AUC<sub>I</sub></i>				
<hr/>							
<i>Salivary cortisol</i>							
<i>Slope</i> (β)		.400**	.596**	.007	.044	.102	.011
<i>AUC<sub>G</sub></i>	.400**		.426**	.394**	.061	.225	-.234
<i>AUC<sub>I</sub></i>	.596**	.426**		.280*	.234	.318*	.159
<hr/>							
Perceived Stress	.007	.394**	.280*		.183	.339*	.131
<hr/>							
Symptoms	.173	.061	.234	.183		.665**	.478**
<hr/>							
Symptom Related Distress	.102	.225	.318*	.339*	.665**		.561**
<hr/>							
Frequency of Strategies	.011	-.234	.159	.131	.478**	.561**	

\*  $p < .05$ , \*\*  $p < .01$

Figure 14.

*Significant Relationships among Stress, Symptoms, Symptom Distress, and Symptom Self-Management*

## Significant Relationships among Stress, Symptoms, Symptom Distress, & Symptom Self-Management



### *Testing the Assumptions of Multiple Regression*

#### *Multicollinearity*

Multicollinearity is a situation in which two or more variables are very closely related linearly. It exists when there is a strong correlation between two or more predictors in a regression model, with the consequence that the true relationship of individual variables with a dependent variable will be wrongly estimated. For example, if two variables are strongly related and are entered into a multiple regression analysis, the relationship of the last one entered is likely to be underestimated. Multicollinearity can be examined using a correlation matrix of all predictors to determine if there is any correlation coefficient between variables that is close to the reliabilities of those variables. Often a criterion of about .80 ( $r > .80$ ) is used (Field, 2005).

Prior to performing the multiple regression analyses, the correlation of predictor variables (salivary cortisol indices -  $AUC_G$ ,  $AUC_I$  and Slope, perceived stress, symptoms, and symptom distress) was examined. The findings showed that there were no notably large correlations among the predictor variables. The correlation coefficients among all predictor variables were less than .70. See Table 19-1 and 19-2.

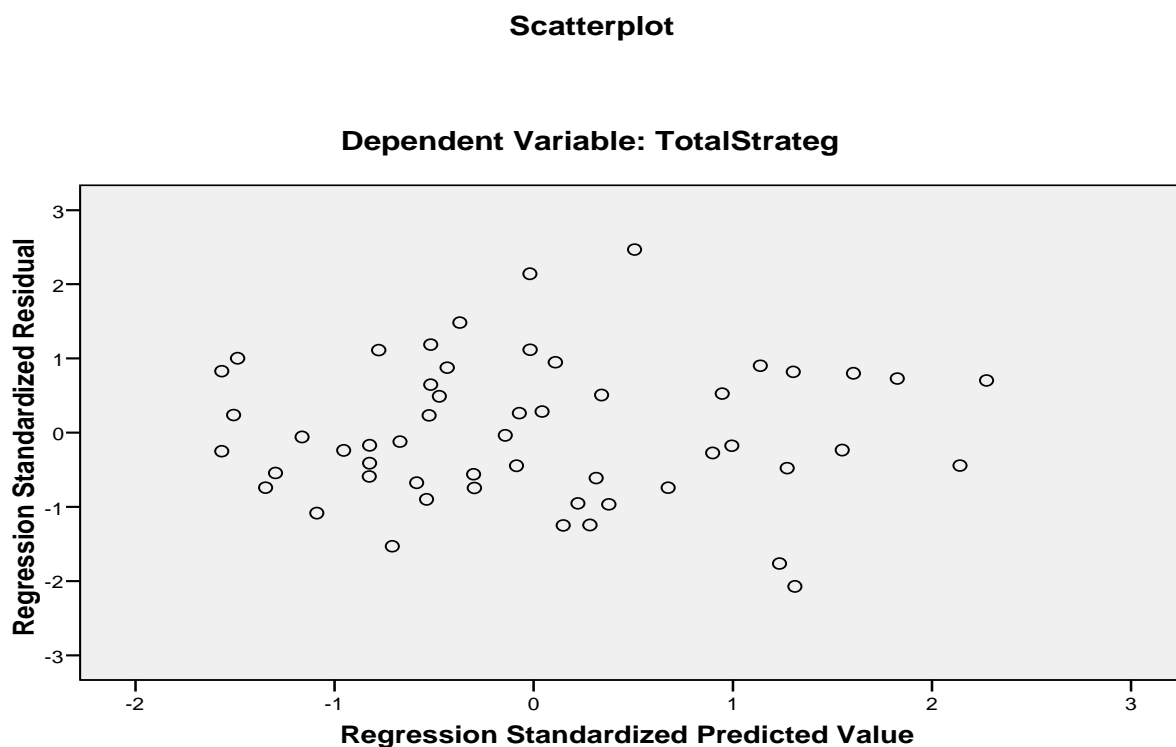
#### *Homoscedasticity*

Homoscedasticity is an assumption in regression analysis that the residuals at each level of the predictor variables should be constant and have similar variance. The accuracy of prediction in a regression model can be detected from residual analysis. Residuals in a regression model are defined as the differences between the values of the outcome predicted by the model and the values of the outcome observed in the sample,

Therefore, if the model fits the sample data well, all residual values will be small (Field, 2005). To check this assumption, the residuals can be plotted against the predicted values (dependent variable) and against the independent variables (predictor variables). Figure 15 shows the points were randomly and evenly dispersed throughout the plot. This pattern indicated that the assumptions of linearity and homoscedasticity were met.

Figure 15.

*Plot of Standardized Residuals against Standardized Predicted Values of the Regression Model of Stress, Symptoms, Symptom Distress, and Symptom Self-Management*

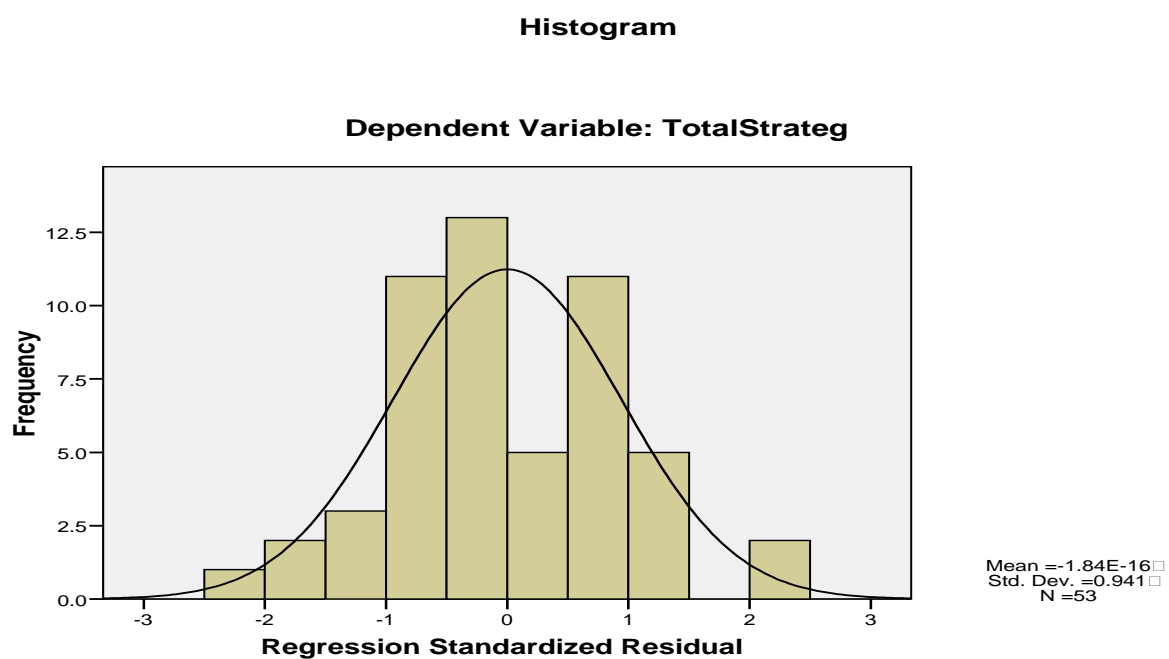


### *Normality*

To test the normality of residuals, a histogram or normal probability plot can be used. All variables were checked for normality by examining the histogram. Salivary cortisol indices were log transformed because of their positive skew. Figure 16 shows the histogram of standardized residuals against standardized predicted values of the regression model of stress, symptoms, symptom distress, and symptom self-management. The distribution may be considered normal.

Figure 16.

*Histogram of Standardized Residuals against Standardized Predicted Values of the Regression Model of Stress, Symptoms, Symptom Distress, and Symptom Self-Management*





### *Outliers and Residuals*

An outlier is a score very different from the rest of the data. From the scatterplot of standardized residuals (Figure 15), there was no outlier. In a normally distributed sample, 95 % of z-scores should lie between  $-1.96$  and  $+1.96$ , 99 % should lie between  $-2.58$  and  $+2.58$ . The standardized residuals with an absolute value greater than 3.29 are cause for concern (Field, 2005). The standardized residual of each case was below 2.5.

### **Research Question Two**

To what extent does stress (salivary cortisol and perceived stress) predict symptoms and symptom distress among patients with localized prostate cancer following radical prostatectomy or radiation therapy?

A multiple regression was performed to determine if stress variables (salivary cortisol and perceived stress) were significant predictors of the symptoms and symptom distress. Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress were entered simultaneously in the first step because they were hypothesized to be the strongest predictors of the symptoms and symptom distress.

Table 20-1 summarizes the multiple regression analysis for salivary cortisol indices (raw data), perceived stress, and symptoms. Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained only 9.3 % of the variance in symptoms,  $F(4, 48) = 1.227$ ,  $p = .312$ . The analysis showed that perceived stress was significantly associated with symptoms ( $\beta = .357$ ,  $p < .05$ ). However, the model was not significant and salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) were not significant predictors of symptoms.

Table 20-2 reveals the hierarchical regression analysis on salivary cortisol indices (log transformed data), perceived stress, and symptoms. Log transformed salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 7 % of the variance in symptoms,  $F(4, 48) = 0.897$ ,  $p = .473$ . The finding showed that the model was not significant; log transformed salivary cortisol indices and perceived stress were not significant predictors of symptoms.

The two analyses showed that salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress were not significant predictors of symptoms.

Table 20-1.

*Summary of Multiple Regression Analyses entering Salivary Cortisol and Perceived Stress as Predictors on Symptoms*

*(Raw Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b>Symptoms</b>							
Step1				.093	.017	.093	.312
Salivary Cortisol							
- AUC <sub>G</sub>	-2.007	1.437	-.266				
- AUC <sub>I</sub>	-.561	.588	-.174				
- Slope	6.649	5.385	.220				
Perceived stress	.535	.253	.357*				

\*  $p < .05$

Table 20-2.

*Summary of Multiple Regression Analyses entering Salivary Cortisol and Perceived Stress as Predictors on Symptoms*

*(Log Transformed Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b>Symptoms</b>							
Step1				.070	-.008	.070	.314
Salivary Cortisol							
- AUC <sub>G</sub>	-.118	.192	-.104				
- AUC <sub>I</sub>	.145	.178	.152				
- Slope	-.194	5.451	-.007				
Perceived Stress	.332	.239	.222				

Table 21-1 summarizes the multiple regression analysis for salivary cortisol (raw data), perceived stress, and symptom distress. Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 14.3 % of the variance in symptom distress,  $F(4, 48) = 1.994$ ,  $p = .110$ . The findings showed that perceived stress was significantly and positively associated with symptom distress ( $\beta = .401$ ,  $p < .05$ ); however, the model was not significant. Salivary cortisol indices were not significant predictors of symptom distress.

Table 21-2 displays the results of the multiple regression analysis on salivary cortisol (log transformed data), perceived stress, and symptom distress. Log transformed salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 16.6 % of the variance for symptom distress,  $F(4, 48) = 2.380$ ,  $p = .065$ . The analyses showed that salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress were not significant predictors for symptom distress, and the model was not significant.

Based on the above findings, two linear regressions were performed to further determine if perceived stress was a significantly strong predictor of symptoms and symptom distress, and how much variance of symptoms and symptom distress can be explained by perceived stress. Two analyses showed that 1) perceived stress was not significantly associated with symptoms ( $\beta = .223$ ,  $p = .108$ ); accounting for 5 % of the variance for symptom distress,  $F(1, 51) = 2.669$ ,  $p = .108$ , and the model was not significant; 2) perceived stress was positively and significantly associated with symptom distress ( $\beta = .343$ ,  $p < .05$ ) accounting for 11.8 % of the variance for symptom distress,  $F(1, 51) = 6.805$ ,  $p < .05$ , and the model was significant.

The analyses showed that perceived stress was a significant predictor of symptom distress, and explained 11.8 % of the variance for symptom distress. See Table 22.

Table 21-1.

*Summary of Multiple Regression Analyses entering Salivary Cortisol and Perceived Stress as Predictors on Symptom Distress (Raw Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b>Symptom Distress</b>							
Step1				.143	.071	.143	.110
Salivary Cortisol							
- AUC <sub>G</sub>	-1.316	1.726	-.141				
- AUC <sub>I</sub>	-.161	.707	-.040				
- Slope	6.537	6.468	.175				
Perceived Stress	.742	.304	.401*				

\*  $p < .05$

Table 21-2.

*Summary of Multiple Regression Analyses entering Salivary Cortisol and Perceived Stress as Predictors on Symptom Distress (Log Transformed Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b>Symptom Distress</b>							
Step1				.166	.096	.166	.065
Salivary Cortisol							
- AUC <sub>G</sub>	.054	.224	.039				
- AUC <sub>I</sub>	.293	.208	.249				
- Slope	-2.297	6.378	-.063				
Perceived Stress	.479	.280	.259				

Table 22.

*Summary of Linear Regression Analyses entering Perceived Stress as Predictors on Symptoms and Symptom Distress (n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b>Symptoms</b>				.050	.031	.050	.108
Perceived Stress	.334	.204	.223				
<b>Symptom Distress</b>				.118	.100	.118	.012
Perceived Stress	.635	.243	.343**				

\*  $p < .05$ , \*\*  $p < .01$



### Research Question Three

To what extent does stress (salivary cortisol and perceived stress) predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

To determine if stress variables (salivary cortisol and perceived stress) were significant predictors of the frequency of symptom self-management strategies, a multiple linear regression was performed. To control for the effect of salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress, they were entered at the same time.

Table 23-1 summarizes the multiple regression analyses entering salivary cortisol and perceived stress as predictors of the frequency of symptom self-management strategies.

Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 14.3 % of the variance in symptom self-management strategies,  $F(4, 48) = 2.010$ ,  $p = .108$ . The model was not significant. The salivary cortisol  $AUC_G$  was significantly and inversely associated with symptom self-management strategies ( $\beta = -.448$ ,  $p < .05$ ).

Table 23-2 reveals that log transformed salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 17.4 % of the variance in symptom self-management strategies,  $F(4, 48) = 2.523$ ,  $p = .053$ . The model was not significant. The log transformed  $AUC_G$  was significantly and inversely associated with symptom self-management strategies ( $\beta = -.432$ ,  $p < .01$ ). The two analyses showed that  $AUC_G$  was significantly and inversely associated with symptom self-management strategies. However, stress variables (salivary cortisol and perceived stress) were not significant predictors of the frequency of symptom self-management strategies.

Table 23-1.

*Summary of Multiple Regression Analyses entering Salivary Cortisol and Perceived Stress as Predictors on the Frequency of Symptom Self-Management Strategies (Raw Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<i>Symptoms Self-Management Strategies</i>							
Step1				.143	.072	.143	.108
Salivary Cortisol							
- AUC <sub>G</sub>	-8.096	3.343	-.448*				
- AUC <sub>I</sub>	-.385	1.369	-.050				
- Slope	13.334	12.524	.184				
Perceived Stress	1.040	.588	.290				

\*  $p < .05$

Table 23-2.

*Summary of Multiple Regression Analyses entering Salivary Cortisol and Perceived Stress as Predictors on the Frequency of Symptom Self-Management Strategies (Log Transformed Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<i>Symptoms Self-Management Strategies</i>							
Step1				.174	.105	.174	.053
Salivary Cortisol							
- AUC <sub>G</sub>	-1.169	.432	-.432**				
- AUC <sub>I</sub>	.720	.401	.315				
- Slope	-.446	12.296	-.006				
Perceived Stress	.671	.540	.187				

\*  $p < .05$ , \*\*  $p < .01$

#### **Research Question Four**

To what extent do symptoms and symptom distress predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

A multiple linear regression was performed to determine if symptoms and symptom distress were significant predictors of symptoms self-management strategies. To control for the effect of symptoms and symptom distress, symptoms and symptom distress were entered at the first step simultaneously.

Table 24 summarizes the multiple regression analyses entering symptoms and symptom distress as predictors of the frequency of symptom self-management.

Symptoms and symptom distress explained 30.7 % of the variance in the frequency of symptom self-management strategies,  $F(2, 50) = 11.602$ ,  $p < .01$ . The analyses showed that the model was significant; symptoms and symptom distress were statistically significant predictors of the frequency of symptom self-management strategies.

Table 24.

*Summary of Multiple Regression Analyses entering Symptoms and Symptom Distress as Predictors on the Frequency of Symptom Self-Management Strategies and the Perceived Effectiveness of Strategies (n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b><i>Symptoms Self-Management Strategies</i></b>							
Step1				.307	.279	.307	.000
Symptoms	.255	.372	.106				
Symptom Distress	.927	.301	.478**				

\*  $p < .05$ , \*\*  $p < .01$

### Research Question Five

To what extent do stress (salivary cortisol and perceived stress), symptoms, and symptom distress predict the frequency of symptom self-management strategies used by patients with localized prostate cancer following radical prostatectomy or radiation?

A hierarchical multiple regression was performed to determine if stress variables (salivary cortisol and perceived stress), symptoms, and symptom distress were significant predictors of symptoms self-management strategies. Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress were selected as the control variable in the first step of the hierarchical regression analyses, followed by symptoms and symptom distress.

Table 25-1 summarizes the hierarchical regression analyses entering stress (perceived stress and salivary cortisol indices), symptoms, and symptom distress as predictors of the frequency of symptom self-management strategies. Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 14.3 % of the variance in the frequency of symptom self-management strategies,  $F(4, 48) = 2.010$ ,  $p = .108$ . The explained variance for the frequency of symptom self-management strategies increased 26.1 % after symptoms and symptom distress were added, and the model became significant,  $F(6, 46) = 5.199$ ,  $p < .01$ . The findings showed that the salivary cortisol  $AUC_G$  was significantly and inversely associated with symptom self-management strategies ( $\beta = -.448$ ,  $p < .05$ ); symptom distress was significantly and positively associated with symptom self-management strategies ( $\beta = .509$ ,  $p < .01$ ); the model was significant by adding symptoms and symptom distress as predictors of symptom self-management strategies.

Table 25-2 presents the hierarchical regression analyses entering log transformed salivary cortisol, perceived stress, symptoms, and symptom distress as predictors of the frequency of symptom self-management strategies. Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) and perceived stress explained 17.4 % of the variance in the frequency of symptom self-management strategies,  $F(4, 48) = 2.523$ ,  $p = .053$ . The explained variance for the frequency of symptom self-management strategies increased 28.3 % after symptoms and symptom distress were added, and the model was significant,  $F(6, 46) = 6.451$ ,  $p < .01$ . The findings showed that the log transformed salivary cortisol  $AUC_G$  was significantly and inversely associated with symptom self-management strategies ( $\beta = -.432$ ,  $p < .01$ ); symptom distress significantly and positively associated with symptom self-management strategies ( $\beta = .556$ ,  $p < .01$ ); the model was significant by adding symptoms and symptom distress as predictors of symptom self-management strategies.

The analyses showed that salivary cortisol  $AUC_G$  and symptom distress were statistically significant predictors of the frequency of symptom self-management strategies. Salivary cortisol  $AUC_I$ , salivary cortisol slope, perceived stress, or symptoms were not significant predictors for the frequency of symptom self-management strategies.

Table 25-1.

*Summary of Hierarchical Regression Analyses entering Salivary Cortisol, Perceived Stress, Symptoms, and Symptom Distress as Predictors on the Frequency of Symptom Self-Management Strategies (Raw Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b><i>Symptoms Self-Management Strategy</i></b>							
Step1				.143	.072	.143	.108
Salivary Cortisol							
- AUC <sub>G</sub>	-8.096	3.343	-.448*				
- AUC <sub>I</sub>	-.385	1.369	-.050				
- Slope	13.334	12.524	.184				
Perceived Stress	1.040	.588	.290				
Step2				.404	.326	.261	.000
Symptoms	.150	.366	.063				
Symptom Distress	.986	.304	.509**				

\*  $p < .05$ , \*\*  $p < .01$



Table 25-2.

*Summary of Hierarchical Regression Analyses entering Salivary Cortisol, Perceived Stress, Symptoms, and Symptom Distress as Predictors on the Frequency of Symptom Self-Management Strategies (Log Transformed Data, n=53)*

Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<i>Symptom Self-Management Strategies</i>							
Step1				.174	.105	.174	.053
Salivary Cortisol							
- AUC <sub>G</sub>	-1.169	.432	-.432**				
- AUC <sub>I</sub>	.720	.401	.315				
- Slope	-.446	12.296	-.006				
Perceived Stress	.671	.540	.187				
Step2				.457	.386	.283	.000
Symptoms	.094	.347	.039				
Symptom Distress	1.077	.297	.556**				

\*  $p < .05$ , \*\*  $p < .01$

A stepwise multiple regression was conducted to explore the largest and significant predictors of the frequency for symptom self-management strategies. Table 26 summarizes the stepwise regression analyses entering stress (salivary cortisol indices and perceived stress), symptoms, and symptom distress as predictors of the frequency of symptom self-management strategies. Symptom distress explained 30 % of the variance in the frequency of symptom self-management strategies,  $F(1, 51) = 21.884$ ,  $p < .01$ . The explained variance for the frequency of symptom self-management strategies increased 12.7 % after log transformed salivary cortisol  $AUC_G$  was added,  $F(2, 50) = 18.635$ ,  $p < .01$ ; the explained variance for the frequency of symptom self-management strategies increased 9.5 % after raw salivary cortisol  $AUC_G$  was added,  $F(2, 50) = 16.342$ ,  $p < .01$ .

The findings showed that symptom distress and salivary cortisol  $AUC_G$  (raw data and log transformed data) were significant predictors ( $\beta = .629$ ,  $p < .01$ ,  $\beta = -.365$ ,  $p < .01$ ,  $\beta = -.309$ ,  $p < .01$ , respectively) of the frequency of symptom self-management strategies. Symptom distress and log transformed salivary cortisol  $AUC_G$  explained 42.7 % of the variance in the frequency of symptom self-management strategies,  $F(2, 50) = 18.635$ ,  $p < .01$ ; symptom distress and raw salivary cortisol  $AUC_G$  explained 39.5 % of the variance in the frequency of symptom self-management strategies,  $F(2, 50) = 16.342$ ,  $p < .01$ . Figure 17 depicts the significant stepwise regression model of the predictions for symptom self-management.

Table 26.

*Summary of Stepwise Multiple Regression Analyses entering Salivary Cortisol Indices, Perceived Stress, Symptoms, and Symptom Distress as Predictors on the Frequency of Symptom Self-Management Strategies (n=53)*

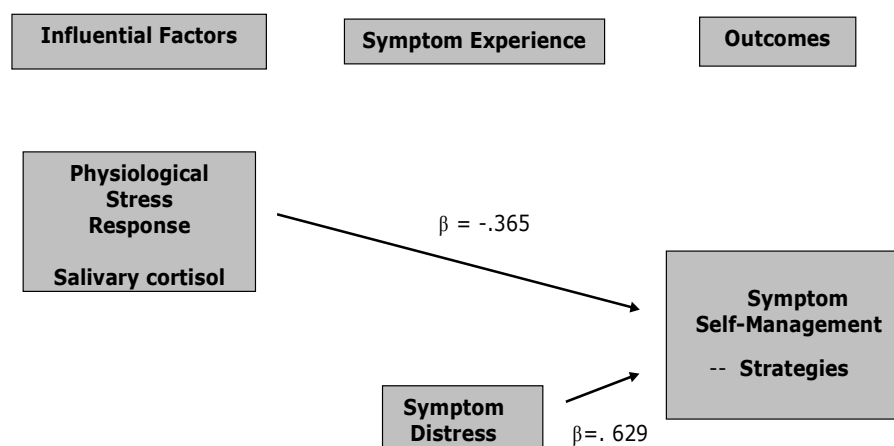
Variable	B	Std. Error	$\beta$	$R^2$	$R^2_{adj}$	$\Delta R^2$	p of $\Delta R^2$
<b><i>Symptom Self-Management Strategies</i></b>							
Model 1				.300	.287	.300	.000
Symptom Distress	1.046	.227	.548**				
Model 2				.427	.404	.127	.002
Symptom Distress	1.218	.213	.629**				
Salivary Cortisol ( <b>Log Transformed Data</b> )							
- AUC <sub>G</sub>	-.989	.297	-.365**				
<b><i>Symptom Self-Management Strategies</i></b>							
Model 1				.300	.287	.300	.000
Symptom Distress	1.046	.227	.548**				
Model 2				.395	.371	.095	.007
Symptom Distress	1.115	.214	.575**				
Salivary Cortisol ( <b>Raw Data</b> )							
- AUC <sub>G</sub>	-5.596	1.996	-.309**				

\*\*  $p < .01$

Figure 17.

*Significant Stepwise Regression Model of the Prediction for Symptom Self-Management*

### Significant Stepwise Regression Model of the Prediction for Symptom Self-Management Strategies



### Summary

This chapter reported the study's results. The psychometric characteristics of the instruments and one biological measure were summarized. Study sample and settings were described. Findings for each research question were presented.

Eight saliva samples and three questionnaires (Perceived Stress Scale, the Symptom Indexes, and the Symptom Self-Management Strategy and Effectiveness) were obtained from each participant between 1 and 3 months following the first treatment for prostate cancer. The sample consisted of fifty-three men with localized prostate cancer, with a mean age of 69 years and 16 years of education.

Salivary cortisol was used as a physiological measure of stress in this study. The areas under the curve ( $AUC_G$  and  $AUC_I$ ), the slope ( $\beta$ ), and the circadian rhythm were calculated to determine levels of physiological stress response. The psychological stress response was measured by the Perceived Stress Scale. The symptoms and symptom distress were measured by the Symptom Indexes. The strategies and perceived effectiveness of symptom self-management were measured by the Symptom Self-Management Strategy and Effectiveness Questionnaire.

Salivary cortisol indices ( $AUC_G$ ,  $AUC_I$  and slope) were calculated for the entire sample and the subgroups on day 1, day 2, and the mean of both days. The radiation therapy group presented a significantly greater  $AUC_I$  than the radical prostatectomy group. However, there was no significant difference in  $AUC_G$  and slope ( $\beta$ ) between the subgroups. Three patterns of circadian rhythms were identified: typical negative circadian rhythm, non-typical flat circadian rhythm, and inconsistent circadian rhythm. The

majority of the sample in this study had a typical, negative, and consistent circadian rhythm. The mean  $AUC_G$  salivary cortisol (raw data and log transformed data) was significantly and inversely associated with symptom self-management strategies in the inconsistent circadian rhythm group. There were no significant differences between the consistent and inconsistent circadian rhythm group on any demographic or study measures.

The perceived stress score was presented for the entire sample and the subgroups. The perceived stress score positively associated with salivary cortisol  $AUC_G$  and  $AUC_I$ . There was no significant difference in perceived stress between the prostatectomy and radiation therapy groups. Symptoms and symptom distress were reported for the entire sample and the subgroups. The total symptoms positively correlated with symptom distress among men with localized prostate cancer following prostatectomy or radiation therapy. The prostatectomy group had a significantly higher score in urinary symptoms and sexual functioning; whereas, the radiation therapy group had a significantly higher score in bowel symptoms.

The frequency and percentage of the symptom self-management strategies and the perceived effectiveness of the strategies were reported and listed by three symptoms (urinary, bowel, and sexual functioning). Symptom self-management strategies positively correlated with symptom self-management effectiveness. The frequency of symptom self-management strategies was significantly and positively correlated with symptoms (severity and frequency) and symptom distress. There were no statistically significant

correlations among the mean slope of salivary cortisol, perceived stress, symptoms, symptom distress, and symptom self-management strategies.

To determine if stress, symptoms, and symptom distress were significant predictors of symptom self-management strategy, a series of multiple linear regressions was performed. The findings showed that symptom distress and salivary cortisol  $AUC_G$  were statistically significant predictors of the frequency of symptom self-management strategies. Symptom distress and log transformed salivary cortisol  $AUC_G$  explained 42.7 % of the variance in the frequency of symptom self-management strategies,  $F(2, 50) = 18.635, p < .01$ ; symptom distress and raw salivary cortisol  $AUC_G$  explained 39.5 % of the variance in the frequency of symptom self-management strategies,  $F(2, 50) = 16.342, p < .01$ . In addition, perceived stress was a significant predictor of symptom distress, and it explained 11.8 % of the variance for symptom distress,  $F(1, 51) = 6.805, p < .05$ .

## CHAPTER V

### DISCUSSION

#### Introduction

In this chapter, the findings from this investigation of stress, symptoms, symptom distress, and symptom self-management in patients with localized prostate cancer will be discussed. The discussion will include: (1) demographic characteristics of the sample, (2) study measures, and (3) the findings from this study. The discussion of the findings will be organized by research aims. Study strengths and limitations will be addressed, implications for practice and research will be discussed, and recommendations for future research will be presented.

#### Discussion of Sample Characteristics

A total of fifty-three patients with localized prostate cancer following radical prostatectomy or radiation therapy were recruited. The mean age of the sample was 68 years ( $SD = 6.9$ ) with a range of 52 to 80 years. The American Cancer Society (2008) estimated that two out of every three men over 65 are diagnosed with prostate cancer (American Cancer Society, 2008), and the median age of prostate cancer diagnosis across all races is 68 years (SEER Cancer Statistics Review, 2008).

The American Cancer Society reported (2008) that prostate cancer is more common in African American men than other races. The majority of this sample were Caucasian 81.2 % ( $n = 43$ ), while 9.4 % was African American ( $n = 5$ ). This ratio is similar to the racial distribution of the local population of this study. According to a 2006 American Community Survey, 63.1 % of the population in Tucson, Arizona was White



and 4.4 % was Black or African American (American Community Survey, 2006). The sample of this study was highly educated with an average of 16 years of education. More than half of the participants were married, no longer employed, and reported incomes that exceeded their expenses.

Twenty-nine participants (55 %) received radiation therapy and twenty-four participants (45%) received radical prostatectomy. The average PSA at the diagnosis was 6.51 ng/ml (SD = 3.1), slightly higher than the normal range (0-4 ng/ml). More than half (54%) of the men with clinically localized prostate cancer had a serum PSA level < 10 ng/ml at the time of diagnosis (Eastham et al., 2008). Treatment was determined by stage and grade of disease at diagnosis, serum PSA levels, results of a digital rectal examine, age at diagnosis, functional status, and life expectancy. Radical prostatectomy and radiation therapy are mainly curative treatment options for early diagnosis of prostate cancer (Bracarda et al., 2005; Eastham et al., 2008; Harlan et al., 2001; Lepore et al., 2003).

#### Discussion of Study Measures

Three questionnaires and one biological measure were used in this study.

##### *Perceived Stress Scale (PSS)*

The 10-item PSS was used to measure psychological stress response, and it showed good reliability. The internal consistency represented by Cronbach's alpha was 0.84. The PSS 10-item questionnaire was easy for participants to understand and generally took 5-10 minutes to complete. This finding was similar to a study of perceived stress in family caregivers of older adults with heart failure in which the PSS

demonstrated to be a brief, easily administered, and highly reliable questionnaire (Cronbach  $\alpha$  0.87, item-total correlations from .4 to .75, no redundant items) (Schwarz & Dunphy, 2003).

### *Symptom Indexes (SI)*

The Symptom Indexes (SI) was used to assess the severity of symptoms and the degree of symptom related distress in localized prostate cancer. The 22-item Symptom Indexes had a good internal consistency (Cronbach  $\alpha$  0.87) in this study. The Symptom Indexes subscale for urinary, bowel, sexual functioning problems, and symptom related distress also had a moderate to high internal reliability (Cronbach  $\alpha$  from 0.6 to 0.8). The psychometric test showed that the Symptom Indexes was a reliable and valid measurement of symptoms and symptom related stress in men with localized prostate cancer who underwent treatments. Clark and Talcott (2001) demonstrated that the Symptom Indexes had good psychometric properties. They concluded that the Symptom Indexes were responsive to treatment effects and were designed to measure symptoms and symptom related distress among patients with early prostate cancer following treatment (Clark & Talcott, 2001).

### *Strategy and Effectiveness of Symptom Self-Management Questionnaire (SESSM)*

The Strategy and Effectiveness of Symptom Self-Management (SESSM) questionnaire was used to measure the frequency of using a strategy to alleviate symptoms (urinary problems, bowel problems, and sexual dysfunction) and the perceived effectiveness of each strategy that was used. This 140-item SESSM had high internal consistency and showed good reliability for the total SESSM questionnaire (Cronbach  $\alpha$

0.92) and the subscale on Strategy (Cronbach  $\alpha$  0.87) and Effectiveness (Cronbach  $\alpha$  0.86).

The SESSM was developed by the researcher based on literature reviews, clinical experiences, and experts' consultations (patients with localized prostate cancer, physicians of radiology oncology and urology, and healthcare professionals in prostate cancer). However, the measurement of symptom self-management strategy and perceived effectiveness was more complex. The Perceived Effectiveness of Strategy subscale could not simply be employed as an outcome measure in this study because of the variety of respondents to symptom self-management strategy. Therefore, the data on the perceived effectiveness of each strategy was analyzed as descriptive data and no correlation or regression analyses with other study measures were performed. However, the SESSM will require further revision to achieve stronger and more stable psychometric properties and before using it with a large sample.

*Biological Measure-Salivary Cortisol: Enzyme-Linked Immunosorbent Assay (ELISA)*

Salivary cortisol was used to indicate the levels of physiological stress response in this study. Salimetrics Expanded Range High Sensitivity (HS) Salivary Cortisol Enzyme Immunoassay was used to measure salivary cortisol. The Salimetrics HS Salivary Cortisol Enzyme Immunoassay had a good sensitivity (0.003  $\mu\text{g/dL}$ ), and the intra-assay coefficients of variation (3.35 % - 3.65 %) and the inter-assay coefficients of variation (3.75 % - 6.41 %) were accurate and reliable. Previous studies reported similar validity and reliability of the measurement kit (Haussmann et al., 2007; Hodgson, Freedman, Granger, & Erno, 2004; Shirtcliff et al., 2001).

Prior to measuring cortisol in saliva, the Salimetrics' Salivary Blood Contamination Enzyme Immunoassay KIT (CN 1-1302/1-1312, 96-Well Kit; Salimetrics, Inc., State College, PA) was used to determine if a saliva sample was contaminated with blood. The kit was a reliable and valid measurement tool. The sensitivity was 0.08 mg/dL, the intra-assay coefficients of variation were 4.9 % to 10.2 %, and the inter-assay coefficients of variation were 9.0 % to 4.1 %. There was no statistically significant difference between salivary cortisol blood contamination and salivary cortisol, so all saliva samples were used to assay salivary cortisol. The findings are consistent with previous studies (Granger et al., 2007; Kivlighan et al., 2004; Schwartz & Granger, 2004).

Saliva samples were collected with sorbette according to the manufacturer's instructions (Salimetrics, 2007) and the protocol to collect saliva samples was followed. It was found that 14 out of 64 samples from eight subjects produced had an insufficient amount of saliva. This might be attributed to the subjects having a dry mouth in the morning from being restricted from drinking water before going to bed. Increasing sorbette from 2 to 4 in collecting the saliva at each single collection might be an alternative way to obtain enough saliva samples.

The quantitative measurement of cortisol in saliva was performed using a cortisol ELISA according to the manufacturer's instructions and procedures (Salimetrics, 2007). Salivary cortisol levels were determined in ug/dL by calculating the mean of duplicate assay results. The ELISA was carried out by the researcher and monitored under a skilled lab technician in the laboratory of the University of Arizona College of Nursing. Haussmann et al. (2007) concluded that ELISA is a modern laboratory tool used to

determine the amount of endogenous antigens in plasma or saliva and can easily be adapted to fit into already existing physiology and endocrinology curriculums (Haussmann et al., 2007).

## Discussion of the Findings Related to Study Aims

### **Research Aim One**

Research Aim One examined physiological and psychological stress responses in men with localized prostate cancer following radical prostatectomy or radiation therapy.

#### *Physiological Stress*

The physiological stress response was measured by salivary cortisol. Samples were obtained at 4 time points over 2 days.

#### *Salivary Cortisol – Mean Concentrations*

As described in Chapter Four, log transformed salivary cortisol and raw salivary cortisol data were used to analyze the relationships between salivary cortisol and study measures (perceived stress, symptoms, symptom distress, and symptom self-management). The results of data analyses comparing log transformed salivary cortisol with raw salivary cortisol data were similar. For clarity, only findings from the analyses of the raw salivary cortisol data are discussed below.

The mean concentrations of salivary cortisol for the entire sample at 4 time points (awakening, noon, afternoon, and evening) over 2 days were 0.306 ug/dL, 0.144 ug/dL, 0.111 ug/dL, and 0.080 ug/dL, respectively. The range of salivary cortisol in this study was lower than the normal range which is from 1.8 ug/dL at the time of awakening to 0.1 ug/dL at the nadir around late evening (Lovallo & Thomas, 2000). Confounding factors

such as unmeasured variables (e.g. exercise, social support, or other medications to decrease cortisol levels such as antidepressant), sample bias, or individual differences could explain the low salivary cortisol concentrations (Ice et al., 2004; Smyth et al., 1997). However, mean cortisol concentrations in this sample were similar to other studies where the normal range of free cortisol in healthy subjects was  $1.0 \pm 0.8$  ug/dL, and 0.6 – 9.3 ug/dL in subjects who were ill (Murray, 1967; Sapse, 1984).

Salivary cortisol levels demonstrated a robust circadian rhythm in which peak levels were found in the early morning hours, with decreasing values thereafter (Sapse, 1984). Cortisol levels were highest in the early morning, decreased during the day, and were lowest late in the day, which is consistent with findings from other studies (Ice et al., 2004; Sephton et al., 2000; Smyth et al., 1997).

The circadian pattern of cortisol secretion was similar in the prostatectomy and radiation therapy groups, although the values were slightly different in the two groups. Interestingly, mean salivary cortisol concentrations were higher in the morning for the prostatectomy group than the radiation therapy group. However the mean salivary cortisol concentrations in the noon, afternoon, and evening for the prostatectomy group were lower than the radiation therapy group. However, there was no statistically significant difference in salivary cortisol concentrations at any time points between the two groups.

#### *Salivary Cortisol – Area under the Curve (AUC)*

There are two types of AUC-area under the curve with respect to ground ( $AUC_G$ ) and area under the curve with respect to increase ( $AUC_I$ ).  $AUC_G$  represented the total

amount of cortisol secreted throughout the day and reflected the basal activity of the hypothalamic-pituitary-adrenal (HPA) axis over the day.  $AUC_I$  represented the sensitivity of cortisol changes over time and reflected reactivity of the HPA axis over the day (Fekedulegn et al., 2007; Pruessner et al., 2003; Vedhara et al., 2006).

Mean total amount of salivary cortisol ( $AUC_G$ ) in this sample was 2.242 ug/dL and the mean value of cortisol changes over time ( $AUC_I$ ) was - 2.346. There is no normal range or standard values for cortisol  $AUC_G$  and  $AUC_I$ . Fekedulegn et al. (2007) proposed that the sign (positive or negative) and magnitude of  $AUC_I$  are associated with various psychological and physical conditions (Fekedulegn et al., 2007). Therefore, negative values of  $AUC_I$  for the entire sample indicated a steady decrease in cortisol levels after the awakening peak response and that there were no significant physical or psychological conditions to increase cortisol secretion after the early morning peak.

$AUC_G$  and  $AUC_I$  of the radiation therapy group were greater than the radical prostatectomy group, indicating that the radiation therapy group had a greater total amount value of salivary cortisol and a higher sensitivity of cortisol changes over time. However, only the difference in  $AUC_I$  between the two treatment groups was statistically significant. This finding could be due to the different psychological or physical conditions experienced by the radiation therapy group. More than half of the participants in the radiation therapy group reported that they received low dose radiation treatments for 10-15 minutes Monday through Friday for 6-8 weeks. Therefore, daily radiation treatment may have been associated with increased psychological or physical conditions and increased cortisol reactivity and secretion in the radiation therapy group.

*Salivary Cortisol – Circadian Rhythm*

The slope of the regression line predicting cortisol concentration at time of day was used to represent each participant's circadian rhythm of cortisol (Smyth et al., 1997). Negative values of the slope were found for the entire sample, indicating that cortisol declined after the early morning peak. The mean salivary cortisol slope of the radiation therapy group was greater than that of the radical prostatectomy group, indicating that the radiation therapy group had slower declines in cortisol compared to the radical prostatectomy group. However, the difference was not statistically significant.

The circadian rhythm represents the pattern of cortisol production over time. Three circadian rhythms were found in this study, which are consistent with previous studies (Smyth et al., 1997). These patterns of cortisol circadian rhythm are typical negative consistent circadian rhythm, non-typical flat consistent circadian rhythm, and inconsistent circadian rhythm (Ice et al., 2004; Smyth et al., 1997; Stone et al., 2001). In this study, the majority of participants (81 %) had a typical, negative consistent circadian rhythm of cortisol, defined as decreasing cortisol levels over the course of the day (Ice et al., 2004; Smyth et al., 1997; Stone et al., 2001). The finding was surprising and unexpected, since there is evidence that HPA function is dysregulated with increasing age (Otte et al., 2005; Sapolsky, Krey, & McEwen, 1986). In addition, previous studies have shown that cortisol dysregulation is associated with the physical stress of cancer (Mormont & Levi, 1997), psychological stressors (Chrousos & Gold, 1998), and psychological distress (McDaniel, Musselman, Porter, Reed, & Nemeroff, 1995).



$AUC_G$  salivary cortisol was significantly and inversely associated with the frequency of symptom self-management strategies ( $r = -.929$ ,  $p < .01$ ) in the inconsistent circadian rhythm group ( $n = 9$ ). No other studies reporting the relationship between inconsistent circadian rhythm and any psychological or physiological measures were found. The study finding suggests that the more stress the subjects in the cortisol inconsistent circadian rhythm group experienced, the fewer symptom self-management strategies they used. In the cortisol consistent circadian rhythm group, there was no significant correlation between salivary cortisol indices and other study measures (perceived stress, symptoms, symptom distress, and symptom self-management).

There were no significant correlations among the salivary cortisol indices (Slope,  $AUC_G$ , and  $AUC_I$ ), other study variables (perceived stress, symptoms, and symptom distress), and demographic characteristics in any of the circadian pattern groups. Smyth and colleagues (1997) conducted a study of individual differences in the diurnal cycle of cortisol and found there were no significant differences between diurnal cycle groups on any demographic or psychological measures (Smyth et al., 1997), which is consistent with the finding of this study.

### *Psychological Stress*

Perceived Stress represented the psychological stress response and was measured by the Perceived Stress scale. The mean score on the Perceived Stress Scale was 9.55 for the entire sample, indicating that low perceived stress was found in men with localized prostate 1-3 months following treatment. The PSS score was lower than U.S. norms for men 65 years of age and older (mean = 12.0, SD = 6.3) (Cohen et al., 1983; Cohen &

Williamson, 1988). This finding is consistent with a study of perceived stress and quality of life among prostate cancer survivors conducted by Joseph et al. These investigators reported that men who had undergone prostatectomy also had low levels of perceived stress (Joseph, Thibault, & Ruttle-King, 2006). Prostate cancer is not always fatal and can be effectually treated (Namiki et al., 2008; Penson, 2007). In addition, more than half of the participants were retired and reported incomes that exceeded their expenses. Therefore, the low level of perceived stress may be due to the nature of prostate cancer and fewer financial concerns among these men.

The radiation therapy group reported higher perceived stress than did the prostatectomy group, but the difference was not statistically significant. No previous studies comparing perceived stress between patients with localized prostate cancer receiving different treatments were found. The radiation therapy group may have had a higher perceived stress due to concerns related to their daily radiation treatments such as travel to out patient radiology departments or rescheduled treatments when the radiation machine was unavailable.

#### *Relationship between Salivary cortisol and Perceived Stress*

Higher perceived stress was significantly and positively associated with salivary cortisol concentrations at noon (11-12 pm) and in the afternoon (4-5 pm). This finding is consistent with previous studies. Smyth et al. (1997) reported that salivary cortisol increased with daily stressors and anticipated stress (Smyth et al., 1997). Several investigators found increased levels of perceived stress were associated with increased concentrations of salivary cortisol (Van Eck & Nicolson, 1994; Vedhara et al., 1999).

Pruessner et al. (1999) demonstrated that perceived stress correlated with increased cortisol levels during the first hour after awakening after dexamethasone pretreatment (Pruessner et al., 1999). However, Lasikiewicz et al. (2008) found neither perceived stress nor daily hassles were significant predictors of cortisol profile (Lasikiewicz et al., 2008).

### **Research Aim Two**

Research Aim Two described the severity and frequency of symptoms and the degree of symptom distress in men with localized prostate cancer following radical prostatectomy or radiation therapy.

Symptoms and symptom distress were measured by the Symptom Indexes. The mean of the total Symptom Indexes was 72.79 for the entire sample, indicating that patients with localized prostate cancer receiving prostatectomy or radiation therapy reported a moderate degree of symptoms and symptom related distress 1-3 months after their first treatment. This finding is similar to several studies where results showed that men with localized prostate cancer experienced moderate to severe symptoms and symptom related distress in urinary, bowel, and sexual functioning after different treatment modalities (Bhatnagar, Stewart, Huynh, Jorgensen, & Kaplan, 2006; Buron et al., 2007; Clark, Bokhour et al., 2003; Clark, Inui et al., 2003; Clark & Talcott, 2001; Korfage et al., 2005; Madalinska et al., 2001; Penson, 2007; Schapira et al., 2001; Talcott et al., 2006).

### *Symptoms*

The mean scores on the Symptoms Subscales (urinary, bowel, and sexual functioning) for the entire sample were 43.19, reflecting moderate symptoms. Urinary problems (urinary incontinence and obstruction) and sexual dysfunction were the most frequent and severe symptoms for these subjects. This is consistent with other studies of health related quality of life or side-effects in early stage prostate cancer after treatment (Buron et al., 2007; Eller et al., 2006; Litwin et al., 2007; Michaelson et al., 2008; Penson, 2007; Perez et al., 1997; Stern & Ippoliti, 2003; Talcott et al., 2003).

The prostatectomy group reported significantly higher mean scores on urinary symptoms and sexual functioning symptoms than did the radiation therapy group. However the radiation therapy group had a higher mean score on bowel symptoms. Damber and Aus (2008) reported that 2 to 100 % of patients with localized prostate cancer receiving radiation therapy experienced moderate to severe gastrointestinal side-effects and the most common and severe side-effects for men treated with radical prostatectomy were erectile dysfunction and urinary incontinence (Damber & Aus, 2008). These findings are also consistent with most studies of health related quality of life in men with early stage prostate cancer treated with radical prostatectomy or radiation therapy. In these studies the prostatectomy group also had greater or more severe urinary symptoms (incontinence, obstruction) and sexual functioning; while the radiation therapy group experienced greater bowel problems (diarrhea, rectal bleeding, or tenderness) (Buron et al., 2007; Clark & Talcott, 2001; Korfage et al., 2005; Madalinska et al., 2001; Penson, 2007; Talcott et al., 2006; Talcott, Clark, Stark, & Mitchell, 2001). However,

Eller et al. reported no treatment group differences in patients' concerns about symptoms (Eller et al., 2006). Eton et al. reported no significant treatment-related differences for bowel function, but men treated with radiation had better urinary function than those treated with prostatectomy (Eton et al., 2001).

### *Symptom Distress*

The mean score on the Symptom Related Distress Subscale was 29.60 for the total sample, suggesting that patients with localized prostate cancer had moderate symptom related distress on urinary, bowel, and sexual dysfunction. Sexual dysfunction had the highest degree of symptom related distress for this sample which is consistent with Litwin's finding that sexual bother was more common than urinary or bowel bother after prostatectomy and radiation therapy (Litwin et al., 2007).

Men with localized prostate cancer receiving radical prostatectomy reported significantly higher total mean scores on the Symptom Related Distress Subscale than did the radiation therapy group. Specifically, the radical prostatectomy group reported higher urinary symptoms distress and sexual dysfunction distress, while the radiation therapy group experienced higher bowel symptoms distress. Only the difference in sexual dysfunction distress between the two groups reached statistical significance. This is consistent with previous studies that also found patients treated with prostatectomy usually had higher distress associated with urinary and sexual functioning, while those treated with radiation therapy had higher bowel problem distress (Bradley et al., 2004; Buron et al., 2007; Clark, Inui et al., 2003; Clark & Talcott, 2001; Henningsohn et al., 2002; Korfage et al., 2005; Litwin et al., 2007; Schapira et al., 2001; Talcott et al., 2003).

Sexual dysfunction distress reported from the prostatectomy group was significantly higher than that of the radiation therapy group. Damber and Aus (2008) documented that 20-100 % of patients with localized prostate cancer treated by prostatectomy developed erectile dysfunction and 0-70 % experienced moderate to severe urinary incontinence (Damber & Aus, 2008). The most common problem after radical prostatectomy was impotence due to the neurovascular bundles involved in penile erections which was damaged during the surgery (Dearnaley et al., 1999; Walsh & Donker, 1982; Walsh, Lepor, & Eggleston, 1983). These may explain why men with localized prostate cancer receiving radical prostatectomy experienced significant sexual functioning problems and sexual dysfunction distress.

*Relationship between Symptoms and Symptom Related Distress*

Pearson's product-moment correlations showed that the Symptoms Subscale was significantly and positively correlated with the Symptom Related Distress Subscale ( $r = .665$ ,  $p < .01$ ), indicating that greater frequency and severity of symptoms was associated with a higher degree of symptom related distress. This is similar to studies that used the Symptom Indexes to assess outcomes of treatment for men with early prostate cancer. Clark and Talcott reported significant correlations between pairs of function (symptoms) and distress indexes ( $r = 0.63-0.84$ ), and between the level of function (symptoms) and patient distress scores (Clark & Talcott, 2001; Talcott et al., 2006). Litwin and colleagues also found that health related quality of life among men treated for early stage prostate cancer was correlated with measures of function and bother in urinary, sexual, and bowel (Litwin et al., 2007; Litwin et al., 1998).

Bowel symptoms were significantly and positively correlated with urinary symptom distress ( $r = .321, p < .05$ ), and sexual dysfunction distress ( $r = .275, p < .05$ ), which is similar to a study that reported that bowel dysfunction (diarrhea, urgency, and pain in bowel movement) was associated with low scores on sexual intimacy and diminished urinary control (Clark, Inui et al., 2003). Urinary symptoms were significantly and positively correlated with sexual dysfunction symptom distress ( $r = .426, p < .01$ ). A qualitative study of perceptions of quality of life and reported urinary incontinence after treatment for early prostate cancer found that patients experienced complex problems including preoccupation with avoiding leakage and the location of bathrooms; and feeling dirty, helpless, and embarrassed when control was lost which might affect their sexual related functioning distress (Clark, Inui et al., 2003). Studies related to quality of life and urinary incontinence after treatment for prostate cancer documented that men who experienced urinary incontinence following prostatectomy felt that it was shameful and unmanly, and was inversely associated with sexual intimacy (Paterson, 2000; Powel, 2000).

### **Research Aim Three**

Research Aim Three described the frequency of strategies for symptom self-management and their perceived effectiveness among men with localized prostate cancer following radical prostatectomy or radiation therapy.

#### *Symptom Self-Management Strategies and Perceived Effectiveness of the Strategy*

Symptom self-management strategies and perceived effectiveness of the strategy were measured by the Strategy and Effectiveness of Symptom Self-Management

(SESSM) questionnaire. Symptom self-management covered three domains of symptoms dysfunction including urinary problems, bowel problems, and sexual dysfunction.

#### *Urinary Symptom Self-Management*

Urinary incontinence and urinary obstruction were the main symptoms of urinary dysfunction in patients with localized prostate cancer following radical prostatectomy or radiation therapy. The strategies perceived to be the most effective to manage symptoms of urinary incontinence were pad or adult diaper, kegel exercise, and endure/tolerate. Other strategies used to alleviate symptoms of urinary incontinence included decrease social activities, take fewer long trips, and avoid drinking water. The most frequent and effective strategies to alleviate symptoms of urinary obstruction were endure/tolerate, take medicines (anticholinergics), kegel exercise, decrease social activities or fewer long trips, and rest.

Overall, kegel exercise was the most frequently used and perceived as the most effective strategy for alleviating urinary symptoms. The mechanism of kegel exercise is to strengthen the pelvic floor muscles which control the urethral sphincter (Moul, 1998; Sueppel, Kreder, & See, 2001). This finding is consistent with some intervention studies related to postprostatectomy in localized prostate cancer which demonstrated that verbal and written information along with telephone support for pelvic floor muscle training and pelvic-floor re-education were effective for managing urinary incontinence (Mathewson-Chapman, 1999; Moore, Valiquette, Chetner, Byrniak, & Herbison, 2007).

Subjects reported that medication (anticholinergics) was also effective to alleviate slow or difficult urination. Only one subject had artificial sphincter surgery. Other



investigators have reported management options for post prostatectomy urinary incontinence including behavioral techniques, pharmacologic therapy (e.g. anticholinergics), surgical intervention (e.g. artificial sphincter insertion), periurethral collagen injection, and other supportive measures (Diokno, 1998; Leach et al., 1996; Mathewson-Chapman, 1999; Moore et al., 2007; Palmer et al., 2003; Van Kampen et al., 2000).

More than half of the participants used “endure and tolerate” as a strategy to deal with the symptoms of urinary incontinence and obstruction, and they perceived it was an effective strategy. Pirl and Mello (2002) reviewed the psychological complications of prostate cancer, and concluded that men with prostate cancer may tend to minimize the impact of the illness on their lives and their need for support (Pirl & Mello, 2002). In addition to the social role of masculinity and social identity, men with urinary incontinence may be reluctant to discuss their problems, leading them to endure or to tolerate the symptoms as a coping strategy.

#### *Bowel Symptom Self-Management*

Men treated with radiation therapy experienced common symptoms of bowel problems such as diarrhea, loose or watery stools, urgency in moving bowels, tenderness or pain, and an urge to move bowels with nothing to pass. The most frequently used strategies to alleviate diarrhea or watery stools included endure/tolerate, rest, eat fruit, drink more water, eat small portions of food, avoid fried or high fiber foods, and take medicines. Subjects perceived that these strategies were effective. No other studies reporting strategies in dealing with bowel problems such as urgency in bowel moves,

tenderness or pain were found. Findings from this study suggests that taking fewer long trips and decreasing social activities were the most effective strategies to alleviate urgency in bowel moves. To endure or tolerate, to rest, not to eat, and to take medicines were the most effective strategies to alleviate symptoms of tenderness or pain.

Previous studies found that stool frequency, rectal pain, urgency, and bleeding were the most common complications in patients with prostate cancer following radiation therapy (Anthony, 2003; Kornblau et al., 2000; Miller et al., 1999; Stern & Ippoliti, 2003). Sten and Ippoliti (2003) summarized the nutritional and dietary guidelines for patients with cancer treatment induced diarrhea including eating small frequent meals slowly; consuming adequate soluble fiber and protein-rich food; drinking ample liquids that are cool or warm not hot or cold; and replacing electrolytes and minerals (Stern & Ippoliti, 2003). Other strategies to alleviate stool frequency, chronic enteritis, or proctitis after high radiation doses included nutritional management (dietary and nutritional guidelines), pharmacologic management (intestinal transit inhibitors and antisecretory agents, or opioids for pain), and surgery (typically required to improve the symptoms of small bowel damage, e.g. severe proctitis) (Anthony, 2003; Kornblau et al., 2000; Miller et al., 1999; Stern & Ippoliti, 2003). These findings are similar to the findings in this study.

#### *Sexual Dysfunction Symptom Self-Management*

Ten strategies were found to alleviate symptoms of sexual dysfunction among men with localized prostate cancer following radical prostatectomy or radiation therapy in this study. The most frequently used and also the most effective strategies were to express their feelings with their partner and to find alternative ways (hug, kiss, touch) to

express their affection. Although decreasing the frequency of sexual activities was one of the most frequently used strategies, it was not an effective strategy. Few participants reported that they had taken medication or consulted a specialist.

Neese and colleagues (2003) conducted a phone survey of men's and women's perspectives on finding help for sexual problems after prostate cancer treatment. They reported twelve strategies for solving sexual problems and found that lack of desire for sex was one of the barriers for men and their partners to seek help for a sexual problem (Neese et al., 2003). Similarly, some of the participants who underwent radiation therapy expressed that they lacked desire to have sex or did not have a partner at that time. These participants did not view not having sex as a problem and expressed that sex was no longer a priority in their lives.

#### *Relationship between the Strategies and the Effectiveness of Strategies*

Correlations between pairs of the frequency of symptom self- management strategies and the perceived effectiveness of strategies were moderate to large ( $r = .524$  to  $.864$ ,  $p < .01$ ). This finding suggests that the strategies participants used to alleviate their symptoms were effective, and the more effective they were, the more frequently they were used. This finding is consistent with a study of symptom self-management and relapse in schizophrenia conducted by Kennedy et al. (2000). Kennedy and colleagues (2000) found that the symptom self-management was significantly correlated with perceived effectiveness of symptom self-management (Kennedy, Schepp, & O'Connor, 2000).

### Research Aim Four

Research Aim Four examined the relationships among stress, symptoms, symptom distress, and symptom self-management among men with localized prostate cancer following radical prostatectomy or radiation therapy.

#### *Relationships among Stress, Symptoms, Symptom Distress, and Symptom Self-Management*

Pearson's product-moment correlations showed that the mean slope of salivary cortisol was significantly and positively correlated with  $AUC_G$  ( $r = .323$ ,  $p < .05$ ) and  $AUC_I$  ( $r = .397$ ,  $p < .01$ ), revealing that the larger the salivary cortisol slope, the greater values of  $AUC_G$  and  $AUC_I$ . This finding suggests that the greater the total amount of salivary cortisol, the higher sensitivity of cortisol changes over time, and the slower the decline in cortisol secretion throughout the day. Vedhara and colleagues proposed that salivary cortisol slope represented the pattern of cortisol production over time;  $AUC_I$  reflected reactivity of HPA axis over the day, while  $AUC_G$  reflected the basal activity of HPA axis over the day. They conducted a study of psychological factors associated with cortisol indices in women with breast cancer and controls and found that  $AUC_G$  was positively correlated with the early morning peak and  $AUC_I$  was negatively correlated with diurnal cortisol. These findings are inconsistent with the findings of this study. These differences might be due to the different sample characteristics and individual differences in cortisol profiles.

$AUC_G$  was significantly and positively correlated with perceived stress ( $r = .410$ ,  $p < .01$ ); this is consistent with several studies which demonstrated that high perceived

stress was associated with elevated cortisol concentrations (Pruessner et al., 1999; Van Eck & Nicolson, 1994). Furthermore, perceived stress was positively correlated with the level of symptom distress ( $r = .339$ ,  $p < .05$ ), indicating that the higher perceived stress the higher degree of symptom distress subjects experienced. This finding is inconsistent with Joseph's study reporting that there were no significant associations among perceived stress, urinary, bowel, or sexual symptoms, and symptom related distress (Joseph et al., 2006).

Symptom self-management strategies were significantly and positively correlated with symptoms ( $r = .478$ ,  $p < .01$ ) and symptom distress ( $r = .561$ ,  $p < .01$ ). Literature supporting the relationships among symptom self-management, symptoms, and symptom distress is sparse. Prior investigators have proposed that physical and psychological symptoms may engender symptom related distress which has the potential to alter quality of life through alterations in self care, physical functioning, symptom management, and treatment tolerance (Portenoy et al., 1994; Watson et al., 1987). However, the finding from this study suggests that the greater the frequency of symptoms, the higher the degree of symptom distress and the greater the use of symptom self-management strategies.

#### *Predictors of Symptoms and Symptom Distress*

When all salivary cortisol indices and perceived stress data were entered into a multiple regression model, perceived stress was found to be a significant predictor of symptoms and symptom distress. None of the salivary cortisol indices ( $AUC_G$ ,  $AUC_I$ , and slope) significantly predicted symptoms or symptom distress. Perceived stress was

significantly and positively associate with symptoms ( $\beta = .357, p < .05$ ) and symptom distress ( $\beta = .401, p < .05$ ); it accounted for 5 % of variance in symptoms and 14.3 % of the variance in symptom distress; however, the model did not reach statistical significance. This might have been related to the small sample size.

#### *Predictors of Symptoms Self-Management*

A series of multiple regressions were performed to determine if stress (salivary cortisol and perceived stress), symptoms, and symptom distress were significant predictors of symptom self-management. It was found that when all salivary cortisol indices (slope,  $AUC_G$  and  $AUC_I$ ), perceived stress, symptom distress, and symptom distress data were entered into the multiple regression model,  $AUC_G$  and symptom distress were significant predictors of symptom self-management.

This finding indicates that  $AUC_G$  was a significant predictor of the frequency of symptom self-management strategies ( $\beta = -.448, p < .05$ ), accounting for 14.3 % variance for symptom self-management. Furthermore, the explained variance for symptom self-management was increased an additional 26.1 % after symptoms ( $\beta = .063, p > .05$ ) and symptom distress ( $\beta = .509, p < .01$ ) were added. Therefore, salivary cortisol  $AUC_G$  and symptom distress were significant and strong predictors of the frequency of strategies for symptom self-management among men with localized prostate cancer. Several studies of health related quality of life in prostate cancer patients reported that symptom distress was an indicator of changes in quality of life (Clark, Inui et al., 2003; Eller et al., 2006; Litwin et al., 2007). Fu and colleagues proposed that symptom occurrence and symptom distress influenced symptom management, and symptom management was related to

quality of life (Fu et al., 2004). Findings of this study suggest that symptom self-management might be sensitive to changes in symptom distress and salivary cortisol among men with localized prostate cancer following treatments.

### *Conceptual Model of Symptom Self-Management*

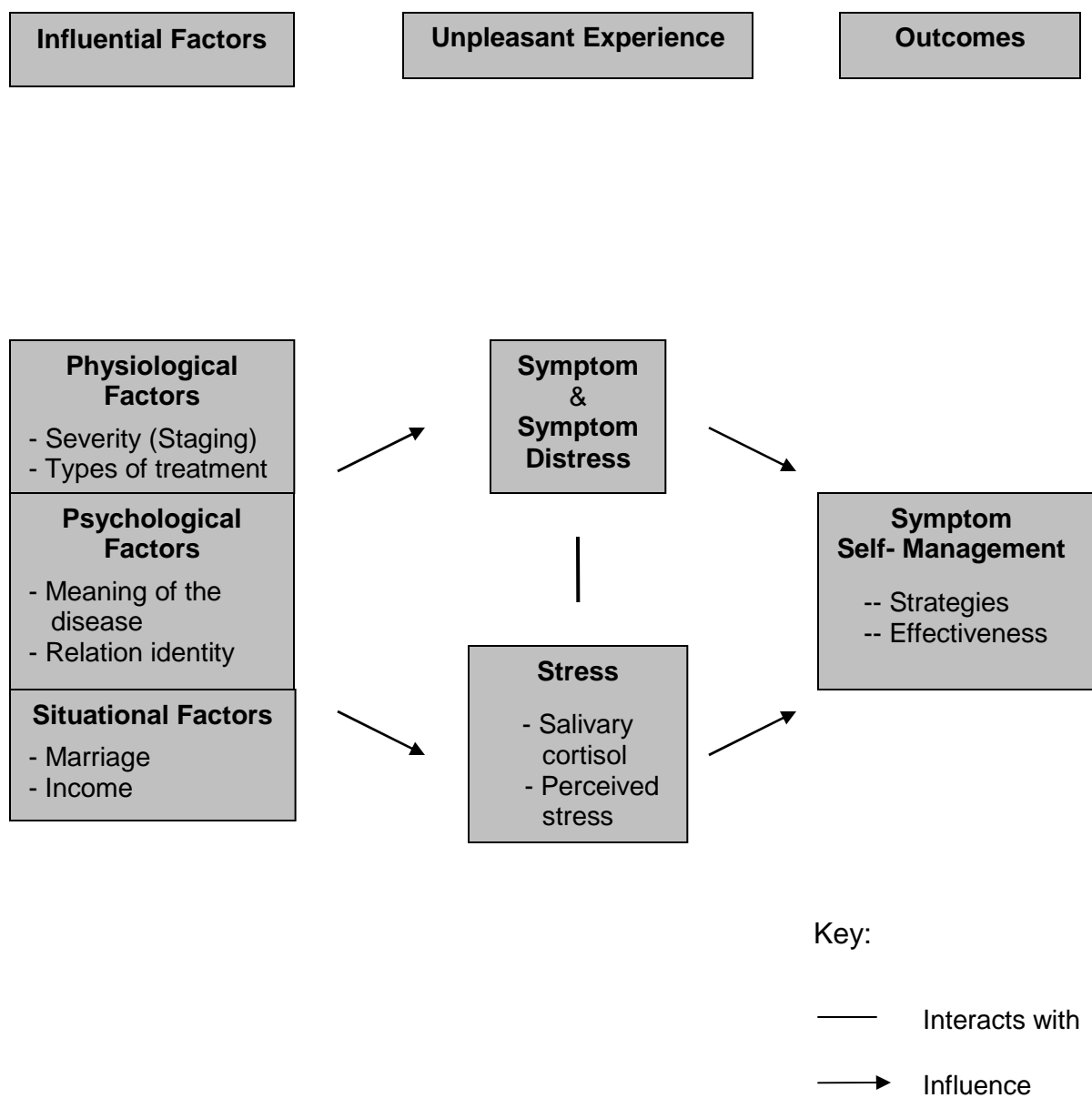
Using Lenz's Theory of Unpleasant Symptoms, a conceptual model of stress, symptoms, symptom distress, and symptom self-management was developed. It was hypothesized that 1) the influential factors (salivary cortisol and perceived stress) and symptom experience (symptoms and symptom distress) had a direct effect on outcomes (symptom self-management); 2) the influential factors had an indirect effect on symptom self-management through symptom experience; and 3) symptom experience had a mediating influence between outcomes (symptom self-management) and the influential factors (salivary cortisol and perceived stress). Findings of this study suggest that 1) the influential factors represented by salivary cortisol only had a direct effect on outcomes (symptom self-management); 2) symptom experience (symptoms and symptom distress) had a direct effect on symptom self-management; and 3) symptom experience (symptoms and symptom distress) did not have a mediating influence between stress and symptom self-management. The conceptual model of symptom self-management based on stress (salivary cortisol and perceived stress), symptoms, and symptom distress was further analyzed. The finding suggests that the influential factors represented by salivary cortisol and symptom experience represented by symptom distress accounted for 40.4 % of the variance for the frequency of symptom self-management strategies.

According to the analysis of the conceptual model of symptom self-management, stress measured by salivary cortisol and perceived stress directly influence the frequency of symptom self-management strategies. Symptoms and symptom distress were significantly associated with the frequency of symptom self-management strategies. In addition, salivary cortisol and symptom distress were significantly strong predictors of the frequency of symptom self-management strategies among men treated with localized prostate cancer. Therefore, the revised conceptual model of symptom self-management is depicted in Figure 18.

In the revised conceptual model, stress, symptoms, and symptom distress are unpleasant experiences. Influential factors include physiological factors (i.e. severity of disease and types of treatment), psychological factors (i.e. meaning of the disease and relation identity), and situational factors (i.e. marriage and income). Some of these variables (e.g. relation identity and meaning of the disease) were not measured in this study, but could be incorporated in future research. Symptom self-management is the outcome of unpleasant experiences; therefore, stress, symptoms, and symptom distress directly influence symptom self-management. In addition, stress, symptoms, and symptom distress are affected by influential factors, and may have a mediating effect between influential factors and symptom self-management.



Figure 18.

*Revised Conceptual Model of Symptom Self-Management*

Finally a stepwise multiple regression was performed to determine the strongest significant predictors of symptom self-management and to find a parsimonious model of the prediction for symptom self-management among men treated for localized prostate cancer. The findings suggest that symptom distress and salivary cortisol  $AUC_G$  were the strongest and most significant predictors of the frequency of symptom self-management strategies ( $\beta = .629, p = .000, \beta = -.365, p = .001$ , respectively). Symptom distress and salivary cortisol  $AUC_G$  explained 39.5 % of the variance in the frequency of symptom self-management strategies ( $F(2, 50) = 18.635, p < .01$ ). Previous studies reporting relationships among salivary cortisol, symptom distress, and symptom self-management in any populations were not found.

### Strengths and Limitations

The strengths and limitations of this study are recognized and described below.

#### Strengths

This study was the first to investigate the relationships among stress (salivary cortisol and perceived stress), symptoms, symptom distress, and symptom self-management in patients with localized prostate cancer 1-3 months following radical prostatectomy or radiation therapy. This study has several strengths. First, the study used salivary cortisol as a biological measure of the physiological stress response to investigate the association between physiological and psychological stress experienced by men with early stage prostate cancer after treatment. Second, the study described symptoms and symptom related distress experienced by men treated with localized

prostate cancer and, particularly, compared the differences in symptoms and symptom distress between the prostatectomy and radiation therapy groups.

Third, this is the first study to survey the frequency of symptom self-management strategies and identify effective symptom self-management strategies used by patients with localized prostate cancer 1-3 months following prostatectomy or radiation therapy. Furthermore, the study first investigated the relationships among salivary cortisol, perceived stress, symptoms, symptom distress, and symptom self-management in men with localized prostate cancer following treatment. A final unique strength is that the study determined the significant and strong predictors of the frequency of symptom self-management strategies for patients with localized prostate cancer 1-3 months after prostatectomy or radiation therapy.

#### Limitations

The limitations of this study should also be recognized. First, the study used a cross-sectional and correlational design. Results can only be interpreted as “associations”, not as “cause and effect”. Second, the generalizability of the findings is limited. The convenience sample was limited to 53 men who were referred by an urologist or radiology oncologist. Subjects were recruited from two medial centers, two urology clinics, and three prostate cancer support groups in central and east Tucson Arizona. More than half of the participants were married, highly educated, no longer employed, and reported incomes that exceeded their expenses. Study results can only be generalized to other patients with localized prostate cancer receiving radical prostatectomy or radiation therapy 1-3 months after their first treatment.

Third, self-administrated questionnaires and self-reports were used in this study. A paper by Williamson (2007) on using self-report measures in neurobehavioral toxicology stated that several issues related to self-report measures such as interpreting questions/responses, recalling relevant information, forming a judgment, formatting a judgment about response alternatives, and reporting the judgment might threaten the validity of self-report measures (Williamson, 2007).

A final limitation was related to the potential difference in subject compliance with the protocol for collecting saliva samples. Several studies discussed the compliance of salivary cortisol sampling (Broderick, Arnold, Kudielka, & Kirschbaum, 2004; Jacobs et al., 2005). These investigators found that data obtained from subjects who were not compliant was significantly different from data obtained from subjects who were compliant with the protocol for collecting saliva samples. This difference was particularly true for interpreting cortisol awakening response, post awakening response, and circadian rhythms (Dockray, Bhattacharyya, Molloy, & Steptoe, 2008). Self-reports of compliance in a salivary cortisol sampling protocol may substantially overestimate actual compliance in the absence of objective monitoring (Broderick et al., 2004). There was no monitoring of participants' compliance with the study protocol for collecting saliva samples in this study. Compliance was maximized by requesting that participants follow the study protocol to record the precise times at which they collected their saliva samples. In addition, a reminder call was made to participants the night before they were scheduled to collect their saliva samples. The results of the salivary cortisol circadian rhythms could have been affected by participants not complying with collecting their saliva samples at

the schedule times. However, the interpretation of cortisol awakening response and post awakening response was not addressed in this study.

### Study Implications

This study aimed to investigate the relationships among stress, symptoms, symptom distress, and symptom self-management and to identify effective strategies of symptom self-management used by men with localized prostate cancer following treatment. The study has implications for nursing practice, nursing science, and nursing research.

### For Nursing Practice

The descriptive findings of stress, symptoms, symptom distress and symptom self-management provide information on 1) how prostate cancer patients perceived or evaluated their situations as being stressful or not stressful, and 2) the levels of stress, the frequency and severity of symptom and symptom distress experienced by men treated with localized prostate cancer 1-3 months after prostatectomy or radiation therapy. This information reinforces the need for health care providers to recognize symptoms and symptom related distress in men treated with localized prostate cancer. For example, health care provider may provide effective interventions for urinary symptoms, sexual dysfunction symptoms and sexual dysfunction distress for patients treated with prostatectomy because the study findings indicated that the prostatectomy group reported significantly greater urinary symptoms, sexual dysfunction symptoms and sexual dysfunction distress. Furthermore, findings revealed that perceived stress was significantly and positively correlated with salivary cortisol, indicating that physiological

stress response was significantly associated with psychological stress response. This evidence helps health care providers to evaluate the stress perceived by patients. Since perceived stress was significantly and positively correlated with salivary cortisol, self report of perceived stress can be used to assess the level of a patient's stress.

The most frequently used and effective strategies to manage symptoms associated with urinary, bowel, and sexual dysfunction for men treated with localized prostate cancer were identified in this study. This information provides a subjective perspective of the strategies prostate cancer patients used for alleviating their symptoms 1-3 following prostatectomy or radiation therapy. It serves as a guide for health care provider to assess the frequency of strategies and to assist patients to find the most effective strategies to alleviate their symptoms based on the treatment patient received. For example, kegel exercise, pad or adult diaper, and endure or tolerate were the most frequently used and effective strategies to alleviate symptoms associated with urinary problems.

#### For Nursing Science

This study employed salivary cortisol as a biological marker to indicate the levels of physiological stress response and to demonstrate the association between physiological stress and psychological stress in men with localized prostate cancer following treatment. The study not only measured the concentrations of cortisol at 4 time points in 24 hours over 2 days, but also demonstrated the typical negative circadian rhythm and the variety of cortisol circadian rhythms in men with localized prostate cancer following radical prostatectomy or radiation. In addition, the finding reveals that salivary cortisol and symptom distress had a direct effect on symptom self-management, and perceived stress

had a direct effect on symptoms and symptom distress. These findings contribute to our understanding of the relationships among salivary cortisol, perceived stress, symptoms, symptom distress, and symptom self-management in localized prostate cancer following treatments.

The updated Theory of Unpleasant Symptoms was chosen to guide the study's conceptual framework. Results of the multiple regression analyses suggest that the hypothesized model did not theoretically fit the study. This could be due to sample characteristics or an incorrect use of stress as an influential factor. However, the updated Theory of Unpleasant Symptoms is a significant nursing model and deserves to be refined and tested in further studies. Understanding the concepts of stress, symptoms, symptom distress, and symptom self-management will assist researchers to choose or construct an applicable theoretical framework for further studies.

#### For Nursing Research

Descriptions of the most frequently used strategies and their highest perceived effectiveness will provide a basis for studying interventions for men with localized prostate cancer to effectively self-manage their symptoms. In addition, the Strategy and Effectiveness of Symptom Self-Management (SESSM) questionnaire was used to measure the frequency of using a strategy to alleviate symptoms and the perceived effectiveness of each strategy used in this study. The SESSM was developed by the researcher based on literature reviews, clinical experiences, and experts' consultations (patients with localized prostate cancer, physicians of radiology oncology and urology, and healthcare professionals in prostate cancer). The SESSM had high internal

consistency and showed good reliability (Cronbach  $\alpha = 0.92$ ) and significant intercorrelations between strategies and effectiveness for symptom self-management ( $r = 0.6-0.8$ ). Though the instrument needs to be tested with a larger sample, the SESSM can be used as an instrument for quantitative research in symptom self-management with prostate cancer patients receiving prostatectomy or radiation therapy.

Finally, this study combined a physiological measure (salivary cortisol) and a psychological measure (perceived stress) to delineate the concept of stress. Salivary cortisol has been widely used in psychobiological and neurobehavioral studies as a biological marker of stress (Levine et al., 2007). Using biological measures can reduce the potential bias in self-report measures (Williamson, 2007). This study suggested that using salivary cortisol to measure physiological stress response was a feasible and practical methodological option for stress related research in Nursing.

#### Recommendations for Future Research

This study examined the relationships among stress, symptoms, symptom distress, and symptom self-management and identified the effective strategies men with localized prostate cancer following prostatectomy or radiation therapy used for symptom self-management. It was the first study to use salivary cortisol as a biological measure of physiological stress in men treated with localized prostate cancer and to examine the associations with perceived stress, symptoms, symptom distress, and symptom self-management in patients with localized prostate cancer. However, some changes are recognized and recommended for further research.



First, further testing of the instrument of the Strategy and Effectiveness of Symptom Self-Management (SESSM) questionnaire is imperative. A structured questionnaire for measuring symptom self-management in patients with localized prostate cancer following treatment was not found, and there are limited qualitative studies reporting strategies used by men with localized prostate cancer to manage urinary incontinence and sexual dysfunction or supportive care (Burt, Caelli, Moore, & Anderson, 2005; Grise & Thurman, 2001; Palmer et al., 2003). The SESSM was first developed to investigate the frequency and the effectiveness of symptom self-management strategies in patients with prostate cancer following treatment. It is important to test the SESSM with a larger sample and to examine the determinants of the frequency of symptom self-management strategies and the effectiveness of the strategies in patients with prostate cancer following different treatments (prostatectomy, radiation therapy, or hormone therapy) in future studies.

Second, it is necessary to find different predictors of symptom self-management for an evidence based practice intervention study. The Theory of Unpleasant Symptoms did not theoretically fit the study's conceptual framework. Findings from this study showed that stress measured by salivary cortisol had a direct effect on symptom self-management and there was no mediator between stress and symptom self-management. Future studies may reconceptualize the model of stress, symptoms, symptom distress and symptom self-management based on the findings from this study. In addition, the Theory of Unpleasant Symptoms may need refinement and testing with different populations to

determine the applicability of the theoretical model and the significant factors related to outcomes.

A final recommendation is related to collecting saliva samples and analyzing salivary cortisol. It was suggested that salivary cortisol assays be run at least in duplicate for each single sample collection (Salimetrics, 2007). The researcher did not assay the saliva samples until more than half of the estimated sample size was obtained. Unfortunately an insufficient amount of saliva had been collected from 14 samples. To avoid a recurrence of this problem, the researcher increased the sorbette (cotton swab) from 2 to 4 in collecting saliva at each single collection, and centrifuged the saliva samples immediately after collecting the samples. According to the manufactory's protocol, the analysis of salivary cortisol required 25 µl of saliva for single determinations. This study used 50 µl of saliva for calculating the mean of duplicate assay results, and an additional 20 µl of saliva was used to test blood contamination prior to measuring salivary cortisol (Salimetrics, 2007).

In summary, this study provides the basis for subsequent studies. The findings need to be replicated in a large sample, interventions to test the effectiveness of self-management strategies are needed, and multivariate studies can refine relevant theories.

### Summary

This cross-sectional study investigated the relationships among stress, symptoms, symptom distress, and symptom self-management and identified effective strategies for symptom self-management in men treated with localized prostate cancer. Stress was measured by salivary cortisol and the Perceived Stress Scale. Symptoms and symptom distress were measured by the Symptom Indexes. Symptom self-management was measured by the Strategy and Effectiveness of Symptom Self-Management questionnaire.

The mean salivary cortisol concentrations for the entire sample ranged from 0.3 to 0.08 ug/dL (early morning to late evening). Cortisol was excreted in a circadian rhythm with heightened activity in the early morning, decreased activity during the day, and lower activity late in the day. The circadian pattern of cortisol secretion was similar in the prostatectomy and radiation therapy groups, although the values were slightly different in the two groups. Salivary cortisol  $AUC_G$  was 2.242 ug/dL and  $AUC_I$  was - 2.346 ug/dL for the entire sample. The negative value of  $AUC_I$  indicated a steady decrease in cortisol levels after the awakening peak response.  $AUC_G$  and  $AUC_I$  of the radiation therapy group were significantly greater than the prostatectomy group, showing that the radiation therapy group had greater total amount values of salivary cortisol and higher sensitivity of cortisol changes over time than did the prostatectomy group.

Three circadian rhythm patterns were found. The majority of the participants had a typical negative consistent circadian rhythm of salivary cortisol.  $AUC_G$  was significantly and inversely associated with symptom self-management strategies in the inconsistent circadian rhythm group. However, there were no significant correlations

among the salivary cortisol indices, other variables (perceived stress, symptoms, and symptom distress), and demographic characteristics in any of the three circadian patterns.

Low perceived stress was found for the entire sample. Perceived stress was significantly and positively correlated with  $AUC_G$ , noon salivary cortisol concentration, and afternoon salivary cortisol concentration. Men treated with prostatectomy or radiation therapy reported a moderate degree of symptoms and symptom distress associated with urinary, bowel, and sexual dysfunction. Urinary problems and sexual dysfunction were the most frequent and severe symptoms. The prostatectomy group reported significantly higher urinary symptoms, sexual dysfunction, and sexual dysfunction distress; while, the radiation therapy group experienced significantly greater bowel symptoms.

The most effective strategies to manage symptoms of urinary incontinence were pad or adult diaper, kegel exercise, and endure/tolerate. The most frequent and effective strategies to alleviate symptoms of urinary obstruction included endure/tolerate, take medicines, and kegel exercise. The most effective strategies to alleviate bowel symptoms included tolerate, rest, eat fruit, drink more water, eat small portions of food, take medicines, take fewer long trips, and decrease social activities. Ten strategies were found to alleviate the symptom of sexual dysfunction. The most effective strategies were express feelings with their partner, find alternative ways to express their affection, and use alternative ways to express sexual intimacy.

The mean slope of salivary cortisol was significantly and positively correlated with  $AUC_G$  and  $AUC_I$ , indicating that the greater the total amount of salivary cortisol, the

higher the sensitivity of cortisol changes over time and the slower the decline in cortisol concentrations throughout the day. Perceived stress was significantly and positively correlated with symptom distress. Symptoms were significantly and positively correlated with symptom distress. The frequency of symptom self-management strategies were significantly and positively correlated with the severity and frequency of symptoms and symptom distress. There were no significant correlations among salivary cortisol slope, perceived stress, symptoms, symptom distress, and frequency of symptom self-management strategies among men with localized prostate cancer in this study.

The conceptual model of symptoms self-management based on the influential factors represented by salivary cortisol and symptom experience represented by symptom distress accounted for 40.4 % of the variance of symptom self-management. Furthermore, a significant stepwise regression model of the prediction for symptom self-management strategy was found. Symptom distress and salivary cortisol  $AUC_G$  were significant and strong predictors of the frequency of symptom self-management strategies, accounting for 39.7 % of the variance in the frequency of symptom self-management strategies. These findings provide a guide for health care providers to develop effective interventions of symptom self-management and to improve the quality of life in patients with localized prostate cancer following prostatectomy or radiation therapy.

APPENDIX A  
HUMAN SUBJECTS REVIEW  
University of Arizona  
And  
Southern Arizona Veterans Affairs Health Care System

Human Subjects Protection Program

THE UNIVERSITY OF  
**ARIZONA**<sup>®</sup>  
 TUCSON ARIZONA

1350 N. Vine Avenue  
 P.O. Box 245137  
 Tucson, AZ 85724-5137  
 (520) 626-6721  
<http://www.irb.arizona.edu>

5 September 2006

Chao-Pin Hsiao, Ph.D. candidate  
 Advisor : Ki Moore, Ph.D.  
 Department of Nursing  
 1305 N. Martin Ave  
 P.O. Box 210203

RE: BSC B06.261 STRESS, SYMPTOM AND SYMPTOM DISTRESS, AND SYMPTOM  
 SELF-MANAGEMENT IN LOCALIZED PROSTATE CANCER

Dear Ms. Hsiao:

We received your research proposal as cited above. The procedures to be followed in this study pose no more than minimal risk to participating subjects and have been reviewed by the Institutional Review Board (IRB) through an Expedited Review procedure as cited in the regulations issued by the U.S. Department of Health and Human Services [45 CFR Part 46.110(b)(1)] based on their inclusion under research category 3, 5 and 7. As this is not a treatment intervention study, the IRB has waived the statement of Alternative Treatments in the consent form as allowed by 45 CFR 46.116(d). Although full Committee review is not required, a brief summary of the project procedures is submitted to the Committee for their endorsement and/or comment, if any, after administrative approval is granted. This project is approved with an **expiration date of 5 September 2007**. Please make copies of the attached IRB stamped consent documents to consent your subjects. **Note: Please provide site authorization to this office from the AzCC prior to recruitment of your subjects from that facility.**

The Human Subjects Committee (Institutional Review Board) of the University of Arizona has a current Federal Wide Assurance of compliance, number FWA00004218, which is on file with the Department of Health and Human Services and covers this activity.

Approval is granted with the understanding that no further changes or additions will be made either to the procedures followed or to the consent form(s) used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee and your College or Departmental Review Committee. Any research related physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely yours,



Theodore J Glatke, Ph.D.  
 Chair, Social and Behavioral Sciences Human Subjects Committee

TJG:pm

cc: Departmental/College Review Committee

**Department of  
Veterans Affairs**

**Memorandum**

Date: July 26, 2007  
From: Chairman Research and Development Service Line (0-151)  
Subj: Project Approval  
To: Robert Krouse, M.D. (2-112)

1. Your research proposal entitled, "Stress, Symptoms and Symptom distress, and Symptoms Self-Management in Localized Prostate," was reviewed, approved and put in HOLD status at the R&D Committee meeting on April 18, 2007.
2. At the time the committee placed this new project in HOLD status since your project entitled, "Detecting Metastasis and Recurrent Colorectal Cancer with Gamma Camera Coincidence Positron Emission Tomography" was in *Lapse Status* with IRB for continuing review.
3. On July 2, 2007 the research administrative office received the approval letter for continuing review from IRB for your project that was in lapse status.
4. As of July 2, 2007, with full compliance with continuing review with the IRB, you have full approval to begin work on this new project.
5. Thank you.

  
Jane Mohler, Ph.D.



APPENDIX B

INFORMED CONSENTS AND HIPPA FORMS

University of Arizona

And

Southern Arizona Veterans Affairs Health Care System

APPROVED BY UNIVERSITY OF AZ IRB  
 THIS STAMP MUST APPEAR ON ALL  
 DOCUMENTS USED TO CONSENT SUBJECTS.  
 DATE: 01-05-06 EXPIRATION: 09-05-07

## Informed Consent

### "Stress, Symptoms and Symptom Distress, and Symptom Self-Management in Localized Prostate Cancer"

#### Introduction

You are being invited to take part in a research study. The information in this form is provided to help you decide whether or not to take part. Study personnel will be available to answer your questions and provide additional information. If you decide to take part in the study, you will be asked to sign this consent form. A copy of this form will be given to you.

#### What is the purpose of this research study?

You are being invited to participate voluntarily in the above-titled research project. The purpose of this project is to learn more about how individuals with prostate cancer experience stress, symptoms and symptom distress after treatment, and to try to find effective strategies to help them manage their symptoms.

#### Why are you being asked to participate?

You are being invited to participate because you have been diagnosed with localized prostate cancer and received radical prostatectomy and/or radiation therapy. You are also invited to participate because you are over 18 years of age, understand and can communicate in English. You have no night-shift work, and do not use medications such as prednisolone or dexamethone.

#### How many people will be asked to participate in this study?

Approximately 80 persons will be asked to participate in this study.

#### What will happen during this study?

You will meet with the Principal Investigator in the Department of Radiology Oncology at the Arizona Cancer Center or the Urology clinic of Dr. Dalkin, or at your house for the initial interview. At the initial interview, the Principal Investigator will explain the study and obtain the consent form from you, and you will be asked to fill out the demographic form which includes the information on your date of birth, ethnic background, education, marriage, income, and medical history such as date of diagnosis and diagnosis, treatment modalities, and PSA levels at diagnosis. At the end of initial interview, you will be given the take home packages which include the device for collecting saliva samples, the schedule for saliva sample collection and the protocol for collecting saliva samples, and 3 questionnaires (Perceived Stress Scale, The Symptom Indexes, and Strategy and

measures, 2) resources related to prostate cancer such as providing information regarding existing social support group for prostate cancer.

**Will there be any costs to me?**

Aside from your time, there is no cost for taking part in this study.

**Will I be paid to participate in the study?**

You will be paid \$ 5 or receive a Chinese lucky symbol chain for your participation.

**Will video or audio recordings be made of me during the study?**

No.

**Will the information that is obtained from me be kept confidential?**

All information associated with the study will be held in confidence. The only persons who will know that you participated in this study will be the Principal Investigator, Chao-Pin Hsiao, Ph.D. Candidate, will have access to the information. You will be assigned a number and that number will be on all documents rather than your name.

Your records will be confidential. You will not be identified in any reports or publications resulting from the study. It is possible that Federal regulators and the University of Arizona Human Subjects Protection Program staff or their designees may have access to the data for compliance purposes. Also, representatives of the Sigma Theta Tau International-Beta Mu Chapter that supports the research study may want to come to the University of Arizona to review your information. If that occurs, a copy of de-identified information may be provided to them.

**What if I am harmed by the study procedures?**

If you are experiencing significant symptoms you will be encouraged to contact the oncologist. The investigator will provide 1) a discussion of symptom self-management with participants after completion of all study measures, 2) offer resources related to prostate cancer such as providing information regarding existing social support group for prostate cancer.

**May I change my mind about participating?**

Your participation in this study is voluntary. You may decide to not begin or to stop the study at any time. Your refusing to participate will have no affect on your treatment. You can discontinue your participation with no affect on your treatment. Also any new information

discovered about the research will be provided to you. This information could have an affect on your willingness to continue your participation.

**Who can I contact for additional information?**

You can obtain further information about the research or voice concerns or complaints about the research by calling the Principal Investigator Chao-Pin Hsiao, Ph.D. Candidate, R.N. at (520) 626-3307. If you have questions concerning your rights as a research participant, have general questions, concerns or complaints or would like to give input about the research and can't reach the research team, or want to talk to someone other than the research team, you may call the University of Arizona Human Subjects Protection Program office at (520) 626-6721. (If out of state use the toll-free number 1-866-278-1455.) If you would like to contact the Human Subjects Protection Program by email, please use the following email address <http://www.irb.arizona.edu/suggestions.php>.

**Your Signature**

By signing this form, I affirm that I have read the information contained in the form, that the study has been explained to me, that my questions have been answered and that I agree to take part in this study. I do not give up any of my legal rights by signing this form.

\_\_\_\_\_  
Name (Printed)

\_\_\_\_\_  
Participant's Signature

\_\_\_\_\_  
Date signed

**Statement by person obtaining consent**

I certify that I have explained the research study to the person who has agreed to participate, and that he or she has been informed of the purpose, the procedures, the possible risks and potential benefits associated with participation in this study. Any questions raised have been answered to the participant's satisfaction.

\_\_\_\_\_  
Name of study personnel

\_\_\_\_\_  
Study personnel Signature

\_\_\_\_\_  
Date signed

APPROVED BY UNIVERSITY OF AZ IRB  
THIS STAMP MUST APPEAR ON ALL  
DOCUMENTS USED TO CONSENT SUBJECTS.  
DATE: 9/5/06 EXPIRATION: 9/5/07

## GUIDELINES FOR SUBJECT AUTHORIZATION FORM FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

### "Stress, Symptoms and Symptom Distress, and Symptom Self-Management in Localized Prostate Cancer"

The United States government has issued a new privacy rule to protect the privacy rights of individuals enrolled in research. The Privacy Rule is designed to protect the confidentiality of an individual's health information. This document hereafter known as an "Authorization for Use and Disclosure of Protected Health Information for Research" describes your rights and explains how your health information will be used and disclosed for this study.

#### PURPOSE

You are being invited to participate voluntarily in the above-titled research project. The purpose of this project is to learn more about how individuals experience and manage their symptoms.

#### USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Health information including diagnosis, date at diagnosis, treatment modalities, and prostate-specific antigen (PSA) levels at the diagnosis will be obtained from the medical chart or provided by you. This information will be used for the study to learn the relationships between symptoms experience and symptom self-management. The Department of Radiology Oncology at the Arizona Cancer Center and the Urology clinic at the Dr. Dalkin office will provide the health information to the Principal Investigator Chao-Pin Hsiao. All study information will be linked with your name for 10 years, and then the link will be destroyed. Access to study information is only limited to the Principal Investigator of this study. You have the right to access your PHI that may be created during this study as it relates to your treatment or payment. Your access to this information will become available only after the study analyses are complete.

#### CONTACTS (Include the following sentences)

You can obtain further information from the Principal Investigator Chao-Pin Hsiao Ph.D. Candidate at (520) 626-3307. If you have questions concerning your rights as a research subject, you may call the Human Subjects Protection Program office at (520) 626-6721.

#### AUTHORIZATION

I hereby authorize the use or disclosure of my individually identifiable health information. I may withdraw this authorization at any time by notifying the Principal Investigator in writing. The address for the Principal Investigator is College of Nursing, University of Arizona, P.O. 210203, Tucson, Arizona 85719. If I do withdraw my authorization, any information previously disclosed cannot be withdrawn and may continue to be used. Once information about me is disclosed in accordance with this authorization, the individual or organization that receives this may redisclose it and my information may no longer be protected by Federal Privacy Regulations. I may refuse to sign this authorization form. If I choose not to sign this form, I cannot participate in the research study. Refusing to sign will not affect my present or future medical care and will

*not cause any loss of benefits to which I am otherwise entitled.* This authorization will expire on the date the research study ends. I will be given a copy of this signed authorization form.

\_\_\_\_\_  
Subject's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Subject

\_\_\_\_\_  
Signature of Subject's Legal Representative (if necessary)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Subject's Legal Representative

\_\_\_\_\_  
Relationship to the Subject



Department of Veterans Affairs

**VA RESEARCH CONSENT FORM**FILE IN CONSENT FORM SECTION OF  
THE MEDICAL RECORD IN DATE ORDER

treatment modalities, and PSA levels at diagnosis. At the end of initial interview, you will be given the take home packages which include the device for collecting saliva samples, the schedule for saliva sample collection and the protocol for collecting saliva samples, and 3 questionnaires (Perceived Stress Scale, The Symptom Indexes, and Strategy and Effectiveness of Symptom Self-Management). It will take 20~30 minutes to finish the initial interview.

At the initial interview, you will be instructed on how to collect saliva sample by using a Salivette device and following the protocol for collecting saliva samples. You will be asked to collect saliva samples 4 times on two consecutive days: on awakening, noon (11 AM -12 PM), afternoon (4 - 5 PM) and evening (9 -10 PM) at your house, during 1-3 months after your first treatment. You will be asked to label each saliva sample with the date and time it was collected and store it in the freezer at your house. It will take 10 minutes to collect each saliva sample for a total of 80 minutes for collecting the 8 saliva samples. You will also be asked to fill out 3 questionnaires including the Perceived Stress Scale, The Symptom Indexes, and Strategy and Effectiveness of Symptom Self-Management Questionnaire the day before you collect saliva samples. It will take 5~10 minutes to fill out each questionnaire for a total of 15~30 minutes for the 3 questionnaires.

On the day before collecting the saliva samples, you will receive a phone call from the Principal Investigator to remind you to fill out the questionnaires and to collect the saliva samples. The Principal Investigator will come to your house to pick up the saliva samples and questionnaires within 7 days after you complete the sample collection.

**RISKS**

The things that you will be doing have no known direct risk to you. It is possible you might feel embarrassed or uncomfortable when you are asked about your symptom experience and symptom self-management, or you could have difficulty following the schedule for collecting the salivary samples. If you feel uncomfortable about reporting the symptoms or symptom self-management, you do not have to answer the questions and you can stop participating immediately. If you have difficulties collecting saliva samples, you can stop participating immediately.

**BENEFITS**

There is no direct benefit to you from your participation. Some people have indicated that participating in nursing research is a satisfying experience. Discussing symptoms and symptom self-management may help you identify more symptom management strategies. You may find the opportunity to respond to questions about symptom management beneficial. The Principal Investigator will also provide 1) a discussion of symptom self-management with participants after completion of all study measures, 2) resources related to prostate cancer such as providing information regarding existing social support group for prostate cancer.

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Department of Veterans Affairs

## VA RESEARCH CONSENT FORM

FILE IN CONSENT FORM SECTION OF  
THE MEDICAL RECORD IN DATE ORDER

In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study investigator at 520-626-3307 during the day or 520-235-0426 after business hours. If you need emergency hospitalization in a private hospital because you are unable to come to the VA, have a family member or friend contact your study doctor so that the VA can coordinate care with the private hospital.

**AUTHORIZATION**

Before giving my consent by signing this form, the methods, inconveniences, risks, and benefits have been explained to me and my questions have been answered. I may ask questions at any time and I am free to withdraw from the project at any time without causing bad feelings or affecting my medical care. My participation in this project may be ended by the investigator or by the sponsor for reasons that would be explained. New information developed during the course of this study which may affect my willingness to continue in this research project will be given to me as it becomes available. This consent form will be filed in an area designated by the Human Subjects Protection Program with access restricted by the principal investigator, Chao-Pin Hsiao, Ph.D. Candidate, RN, or authorized representative of the Nursing Department. I do not give up any of my legal rights by signing this form. A copy of this signed consent form will be given to me.

\_\_\_\_\_  
Subject's Signature\_\_\_\_\_  
Date\_\_\_\_\_  
Parent/Legal Guardian (if necessary)\_\_\_\_\_  
Date\_\_\_\_\_  
Witness (if necessary)\_\_\_\_\_  
Date**INVESTIGATOR'S AFFIDAVIT**

Either I have or my agent has carefully explained to the subject the nature of the above project. I hereby certify that to the best of my knowledge the person who signed this consent form was informed of the nature, demands, benefits, and risks involved in his/her participation.

\_\_\_\_\_  
Signature of Presenter\_\_\_\_\_  
Date\_\_\_\_\_  
Signature of Investigator\_\_\_\_\_  
Date

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## APPENDIX C

## PROTOCOL FOR COLLECTING SALIVA SAMPLES

*PROTOCOL FOR COLLECTING SALIVA SAMPLES*

***Time:***

Collect sample at the time of 1) awakening (before getting out of bed), 2) 11~12 pm (around noon), 3) 4~5 pm (afternoon), and 4) 9~10 pm (evening) for 2 day sequentially.

***Note:***

1. Do not brush teeth or consume any alcohol 30 minutes before collecting the saliva.
2. Do not eat meals, foods, or snacks 30 minutes before collecting the saliva.
3. Rinse mouth with water 10 minutes before collecting the saliva.

***Procedure:***

1. Before getting out of bed, please collect the first sample when you wake up (open your eyes) in the morning.
2. Place one cotton stick (swab) in mouth, under tongue, at least for 1-2 minutes.
3. Put the saturated cotton stick (swab) in the plastic tube.
4. Place another cotton stick (swab) in mouth, under tongue, for 1-2 minutes.
5. Put the saturated cotton stick (swab) in the special plastic tube (**2 saturated cotton sticks should be placed in a color coded plastic tube for each collection**).
6. Mark the plastic tube with the time and the date (or put the color sticker on the tube that indicates the time and the date for collecting saliva).

***Note:***

1. Inspect for visible blood contamination, if contaminated; please make a note of it.
2. Make a daily log to explain if there is anything unusual happening during the day with collecting sample (e.g. unexpected visitor or phone call...)

***Store:***

1. Store the saliva samples in the freezer at your house.
2. I will come to your house to pick up the sample in 7 days after you complete all sample collections.

***I deeply appreciate with your co-ordination and help.  
THANK YOU VERY MUCH!!***

APPENDIX D  
PERCEIVED STRESS SCALE

ID # \_\_\_\_\_

**Perceived Stress Scale- 10 Item**

Instructions: The questions in this scale ask you about your feelings and thoughts in the past week. In each case, please indicate with a check how often you felt or thought a certain way.

1. In the past week, how often have you been upset because of something that happened unexpectedly?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

2. In the past week, how often have you felt that you were unable to control the important things in your life?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

3. In the past week, how often have you felt nervous and "stressed"?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

4. In the past week, how often have you felt confident about your ability to handle your personal problems?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

5. In the past week, how often have you felt that things were going your way?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

6. In the past week, how often have you found that you could not cope with all the things that you had to do?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

7. In the past week, how often have you been able to control irritations in your life?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

8. In the past week, how often have you felt that you were on top of things?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

9. In the past week, how often have you been angered because of things that were outside of your control?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

10. In the past week, how often have you felt difficulties were piling up so high that you could not overcome them?

\_\_\_0=never \_\_\_1=almost never \_\_\_2=sometimes \_\_\_3=fairly often \_\_\_4=very often

APPENDIX E  
SYMPTOM INDEXES

ID # \_\_\_\_\_

**The Symptom Indexes****Urinary Problems**1. **In the past week**, how easy has your urine flow been?

Very easy	Fairly easy	Slow, but I don't have to strain or bear down	Slow, and I do have to strain or bear down	Very slow, and I have to strain or bear down hard
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

2. **In the past week**, how often did you urinate at night?

Seldom or never	Once a night	2 to 3 times a night	More than three times a night
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>

3. **In the past week**, how often did you urinate?

4 or fewer times a day	5 to 8 times a day	9 to 12 times a day	More than 12 times a day
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>

4. **In the past week**, how often have you felt pain or burning during urination?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

5. **In the past week**, how often did you have the feeling that it is urgent that you pass your urine?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

6. **In the past week**, how much control did you have over your urine?

Had complete control (no leaking)	Leaked urine, but only at certain times	Leaked urine most of the time	Little or no control
1	2	3	4

7. **In the past week**, how often did you leak urine?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
1	2	3	4	5

8. **IF YOU LEAKED URINE IN THE PAST WEEK**, how much usually comes out?

Had complete control (no leaking)	A few drops	Less than a tablespoon	More than a tablespoon	Can't tell how much
1	2	3	4	5

9. In the past week, how distressed or worried have you been about each of the following?

	Not at all	Slightly	Moderately	Quite a bit	Extremely
Leaking urine	1	2	3	4	5
Slow or difficult urine flow	1	2	3	4	5
Urinating at night	1	2	3	4	5
Frequent urination	1	2	3	4	5
Pain or burning during urination	1	2	3	4	5
Urgency in urination	1	2	3	4	5



<b>Bowel Problems</b>
-----------------------

**The questions in this section ask about bowel problems that may be caused by various physical conditions.**

10. **In the past week**, how often did you have diarrhea, or loose, watery stools?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

11. **In the past week**, how often did you have a sense of urgency that you move your bowels?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

12. **In the past week**, how often did you have tenderness or pain when you move your bowels?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

13. **In the past week**, how often did you have bleeding with your bowel movements?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

14. **In the past week**, how often did you have abdominal cramping or pain?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

15. **In the past week**, how often did you have the feeling that you have an urge to move your bowels, but have nothing to pass?

Not at all	Occasionally	Fairly frequently	Frequently	Very frequently
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

16. In the past week, how distressed or worried have you been about each of the following?

	Not at all	Slightly	Moderately	Quite a bit	Extremely
Diarrhea or loose, watery stools	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
Urgency in moving your bowels	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
Tenderness or pain when you move your bowels	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
An urge to move your bowels with nothing to pass	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

### Sexual Functioning

17. **In the past 4 weeks**, what is the most erect (or hard) your penis has become at any time?

Full erection	Nearly full erection - sufficient for penetration without manual assistance	Partial erection - capable of penetration with manual assistance	Partial erection - not capable of penetration even with manual assistance	No erection at all
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

18. **In the past 4 weeks**, how much difficulty have you had getting an erection during sexual activity?

A lot	Some	A little	No difficulty	Have not had sexual activity
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

19. **In the past 4 weeks**, how much difficulty have you had keeping an erection during sexual activity?

A lot	Some	A little	No difficulty	Have not had sexual activity
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>

20. **In the past 4 weeks**, have you been able to reach orgasm (sensation of climax)?

Yes, all the time	Yes, some of the time	No, not at all	Have not engaged in sexual activity in the past 4 weeks
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>

21. **In the past 4 weeks**, have you been able to ejaculate?

Yes, all the time	Yes, some of the time	No, not at all	Have not engaged in sexual activity in the past 4 weeks
1	2	3	4

### MOS Sexual Problems Scale

22. How big a problem, if any, has each of the following been for you during **the past four weeks**?

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Your level of sexual desire	1	2	3	4	5
b. Your ability to relax and enjoy sex	1	2	3	4	5
c. Your ability to become sexually aroused	1	2	3	4	5
d. Your ability to have an erection	1	2	3	4	5
e. Your ability to reach orgasm	1	2	3	4	5

APPENDIX F

STRATEGY AND EFFECTIVENESS OF SYMPTOM SELF-MANAGEMENT

QUESTIONNAIRE

### Strategy and Effectiveness of Symptom Self-Management Questionnaire

This is the questionnaire that will help us know what strategies you use or used before to manage the symptoms you experienced; and how effective the strategies have been.

**Frequency** (How often have you used the strategy? 0 = Never use, 1= seldom, 2 = sometimes, 3 = very often)

**Effectiveness** (How effective have the strategies been? 0 = not at all, 1= slightly, 2 = moderately, 3 = extremely)

Symptoms	Strategies	Frequency				Effectiveness			
		0	1	2	3	0	1	2	3
<b>Urinary Problems</b> - Leaking urine	1. Use pad or adult diaper	0	1	2	3	0	1	2	3
	2. Take medicines	0	1	2	3	0	1	2	3
	3. Decreased social activities	0	1	2	3	0	1	2	3
	4. Fewer long trips	0	1	2	3	0	1	2	3
	5. Endure/Tolerate (did not use any strategies but tolerate or endure)	0	1	2	3	0	1	2	3
	6. Other strategies	0	1	2	3	0	1	2	3

Symptoms	Strategies	Frequency				Effectiveness			
		0	1	2	3	0	1	2	3
<b>Urinary Problems</b> -Slow or difficult urine flow	1. Take medicines	0	1	2	3	0	1	2	3
	2. Endure/Tolerate	0	1	2	3	0	1	2	3
	3. Other strategies	0	1	2	3	0	1	2	3
<b>Urinary Problems</b> - Urinating at night	1. Use pad or adult diaper	0	1	2	3	0	1	2	3
	2. Avoid drinking water before going to bed	0	1	2	3	0	1	2	3
	3. Take medicines	0	1	2	3	0	1	2	3
	4. Endure/Tolerate	0	1	2	3	0	1	2	3
	5. Other strategies	0	1	2	3	0	1	2	3
<b>Urinary Problems</b> - Frequent urination	1. Use pad or adult diaper	0	1	2	3	0	1	2	3
	2. Take medicines	0	1	2	3	0	1	2	3
	3. Decreased social activities	0	1	2	3	0	1	2	3
	4. Fewer long trips	0	1	2	3	0	1	2	3
	5. Endure/Tolerate	0	1	2	3	0	1	2	3
	6. Other strategies	0	1	2	3	0	1	2	3

Symptoms	Strategies	Frequency				Effectiveness			
		0	1	2	3	0	1	2	3
<b>Urinary Problems</b> - Pain or burning during urination	1. Take medicines	0	1	2	3	0	1	2	3
	2. Rest	0	1	2	3	0	1	2	3
	3. Endure/Tolerate	0	1	2	3	0	1	2	3
	4. Other strategies	0	1	2	3	0	1	2	3
<b>Urinary Problems</b> - Urgency in urination	1. Use pad or adult diaper	0	1	2	3	0	1	2	3
	2. Take medicines	0	1	2	3	0	1	2	3
	3. Decreased social activities	0	1	2	3	0	1	2	3
	4. Fewer long trips	0	1	2	3	0	1	2	3
	5. Endure/Tolerate	0	1	2	3	0	1	2	3
	6. Other strategies	0	1	2	3	0	1	2	3



Symptoms	Strategies	Frequency				Effectiveness			
		0	1	2	3	0	1	2	3
<b>Bowel Problems</b> - Diarrhea or loose, watery stools	1. Try a clear liquid diet	0	1	2	3	0	1	2	3
	2. Avoid fried foods	0	1	2	3	0	1	2	3
	3. Avoid high fiber foods	0	1	2	3	0	1	2	3
	4. Eat frequent, small meals	0	1	2	3	0	1	2	3
	5. Do things to shift attention (away from problem)	0	1	2	3	0	1	2	3
	6. Drink more water	0	1	2	3	0	1	2	3
	7. Eat fruits	0	1	2	3	0	1	2	3
	8. Eat small portions of food	0	1	2	3	0	1	2	3
	9. Endure/Tolerate	0	1	2	3	0	1	2	3
	10. Rest	0	1	2	3	0	1	2	3
	11. Take medicines	0	1	2	3	0	1	2	3
	12. Other strategies	0	1	2	3	0	1	2	3
<b>Bowel Problems</b> - Urgency in moving your bowels	1. Use pad/adult diaper	0	1	2	3	0	1	2	3
	2. Decreased social activities	0	1	2	3	0	1	2	3
	3. Fewer long trips	0	1	2	3	0	1	2	3
	4. Other strategies	0	1	2	3	0	1	2	3

Symptoms	Strategies	Frequency				Effectiveness			
		0	1	2	3	0	1	2	3
<b>Bowel Problems</b> - Tenderness or pain	1. Endure/Tolerate	0	1	2	3	0	1	2	3
	2. Do things to shift attention (away from pain)	0	1	2	3	0	1	2	3
	3. Not eat	0	1	2	3	0	1	2	3
	4. Massage	0	1	2	3	0	1	2	3
	5. Rest	0	1	2	3	0	1	2	3
	6. Take medicines	0	1	2	3	0	1	2	3
	7. Other strategies	0	1	2	3	0	1	2	3
<b>Bowel Problems</b> - An urge to move bowels with nothing to pass	1. Use pad / adult diaper	0	1	2	3	0	1	2	3
	2. Decreased social activities	0	1	2	3	0	1	2	3
	3. Fewer long trips	0	1	2	3	0	1	2	3
	4. Other strategies	0	1	2	3	0	1	2	3

Symptoms	Strategies	Frequency				Effectiveness			
		0	1	2	3	0	1	2	3
<b>Sexual Functioning</b> - Sexual desire - Ability to relax and enjoy sex - Ability to have an erection - Ability to reach orgasm - Ability to penetrate	1. Express feelings with partner	0	1	2	3	0	1	2	3
	2. Express decreased sexual desire with partner	0	1	2	3	0	1	2	3
	3. Decreased frequency of sexual activity	0	1	2	3	0	1	2	3
	4. Find alternative ways (hugging, kissing, touching) to express affection	0	1	2	3	0	1	2	3
	5. Find alternative ways (hugging, kissing, touching) to express sexual intimacy	0	1	2	3	0	1	2	3
	6. Find alternative ways (hugging, kissing, touching) to bring each to orgasm	0	1	2	3	0	1	2	3
	7. Take medicines	0	1	2	3	0	1	2	3
	8. Consult therapist or sexual professional	0	1	2	3	0	1	2	3
	9. Other strategies	0	1	2	3	0	1	2	3

APPENDIX G  
DEMOGRAPHIC FORM

1. What is your birth day? Month \_\_\_\_ Day \_\_\_\_ Year \_\_\_\_
2. What is your ethnic background? \_\_\_\_\_
3. How many years of education have you completed? \_\_\_\_\_ Years
4. Marriage: \_\_\_\_ never married \_\_\_\_ married \_\_\_\_ living with significant other  
\_\_\_\_ separated \_\_\_\_ widowed \_\_\_\_ divorced
5. Are you retired? Yes \_\_\_\_ ( Job \_\_\_\_\_ ) No \_\_\_\_
6. Income: Check the statement that best describes your financial situation  
\_\_\_\_ My income exceeds my expenses; I have no trouble paying my bills.  
\_\_\_\_ My income meets my expenses, I pay my bills.  
\_\_\_\_ My income barely meets my expenses; I have little money left over  
after paying my bills.  
\_\_\_\_ My income does not meet my expenses; I usually cannot pay my bills  
on time.
7. How long have you had this diagnosis? \_\_\_\_\_ Years \_\_\_\_\_ Months  
(OR when you were diagnosed with prostate cancer? \_\_\_\_\_ Month/Year
8. What is your PSA level when you were diagnosed with disease? \_\_\_\_\_
9. Which treatments have you been received?  
\_\_\_\_ Radical Prostatectomy (when? \_\_\_\_ Year \_\_\_\_ Month)  
\_\_\_\_ Radiation Therapy (when? \_\_\_\_ Year \_\_\_\_ Month)  
\_\_\_\_ Radical Prostatectomy and Radiation Therapy  
(When? \_\_\_\_ Year \_\_\_\_ Month for RP;  
\_\_\_\_ Year \_\_\_\_ Month for RT)

APPENDIX H  
STUDY FLYER

## **STUDY PARTICIPANTS NEEDED**

**We're looking for:**

**“MEN WITH LOCALIZED PROSTATE CANCER WHO  
HAVE RECEIVED RADICAL PROSTATECTOMY,  
RADIATION THERAPY OR CRYOTHERAPY”**

This is a study of stress, symptoms and symptom distress, and symptom self-management in localized prostate cancer. The goal of the study is to learn how men with prostate cancer manage their symptoms after treatment, and to try to find effective strategies to help them manage their symptoms.

If you have been diagnosed with prostate cancer and treated with radical prostatectomy, radiation therapy, or cryotherapy; can read and understand English.

**IF YOU WOULD LIKE TO SHARE YOUR EXPERIENCES  
AND BE PART OF THIS STUDY**

**PLEASE CALL: Ms. Chao-Pin Hsiao**, a graduate student,  
At **520-626-3307; 520-235-0426**

Compensation Provided

The University of Arizona College of Nursing

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