Sleep Disruption and Interstitial Cystitis Symptoms in Women

A Thesis

Submitted to the Faculty

of

Drexel University

by

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in partial fulfillment of the

requirements for the degree

of

Doctor of Nursing Practice

March 2009
Dedications

To my husband Paul and my boys Nicholas and Christopher,

I could never put in words how important you are to me.
Acknowledgements

Obtaining a doctorate is like raising a child, it takes a village. I have many people to thank for helping me with this process. First of all I have to acknowledge and thank Judith Reishtein, my supervising professor and mentor. She has helped me through the highs and the lows of this journey. None of this would have been possible without her hard work and dedication to my success. Many times she worked weekends, nights and even during her vacation to prompt, prod, and perfect my work. I am so lucky to have been able to work with her, as she and I complemented each other wonderfully. Specifically I want to thank her for her unique firefighter abilities. I say this because she has this very tall ladder which she would pull out to reach me while I was clinging to the ceiling on many stressful occasions. She had a great way of coaxing me off that ceiling and back down to earth. Saying thank you just does not seem to be enough. Her actions will be remembered for a lifetime. I will work hard every day to ensure I reflect on her in a positive manner.

To my illustrious committee members, thank you for all your time and feedback. Lily Arya, we have known each other for a while and I am so glad that you participated in this journey. Although you may not have known it, it was you who I emulated on balancing a family with a successful career. Thank you for providing me with a well balanced role model.
I would not have even known about the Drexel program without Joan Bloch passing the word along. As my first advisor she and I and baby Christopher would walk in circles around the mall while having our quarterly meetings. Her support and acceptance of my real life was a gift that I needed during this journey. I am very lucky to have you in my life. Trish Shewokis went above and beyond what any fourth reader would have done. Her expertise in statistics refined and strengthened my work more than I could have ever imagined. I thank her so much for opening her door to me, for her time, and her commitment to my research.

The juggling act that has been the past few years of my life would not have possible without the help of Connie and Carl, my wonderful in-laws, who I am truly blessed to have in my life and who I love so very much. Their flexibility of schedule and willingness to always help out is a true testament to their love and support for me and my family.

I would not have even known about this extraordinary program let alone applied for it without Kym Elles-Montomery. She has been my right arm through this journey sharing in my triumphs and tragedies. I would have never made it through without her. The story of how she and I made it into this program will be told and retold unto a ripe old age.
Kristen VanIderstyne is a young lady, wise beyond her years. As our family babysitter and neighbor she has helped since the beginning of this journey. Giving me time to write and study and helping out in a moment’s notice. Her kindness and selflessness will always be remembered.

My friends, you know who you are. For the past few years you have been by my side through this journey. You were there with kind words and motivation and dinners and wine. You took my family out so I could write and took me out to maintain my sanity. I thank you for all your acts of kindnesses as they will always be remembered.

Lucredia Perilli and the ICA were instrumental in my data collection. So kindly they offered to help facilitate my study and graciously shared in my excitement as recruitment commenced.

Although I will never know who they are, none of this could have been possible without my study participants. They generously offered themselves; as one person commented, “What a blessing to feel that I might in some small way help validate someone's experience with the horrors of trying to live a normal life with such abnormal conditions 24/7. Thank you for this place of honor, which I have done nothing to earn except having the unfortunate life challenge of living with such chronic pain without knowing the true etiology.”

The blessing was surely mine.
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Abstract

Sleep Disruption and Interstitial Cystitis Symptoms in Women
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INTRODUCTION: Interstitial cystitis (IC) is a chronic painful disorder of the bladder of unknown etiology and with no known cure. It affects 1.2 million women in United States. The primary symptoms include urinary frequency, urgency and pain the mean age of diagnosis is 40 years. This disorder has been shown to cause many adverse effects in the lives of people who have it. However there is a gap in literature regarding sleep issues in IC patients and how sleep affects the symptoms of IC. This causes confusion and inconsistencies in treating people with IC and sleep disturbances. The goal of this project was to provide a scientific base for evaluation and treatment of sleep difficulties in this population.

METHODS: This cross-sectional descriptive study recruited IC patients (N=407) through the website of the Interstitial Cystitis Association. All subjects completed a web-based questionnaire which included demographic variables, as well as number of years with IC diagnosis, method of diagnosis, type of specialist who made the diagnosis, and menopause status. Depressive symptoms
were measured using a single question, and the O’Leary Sant IC Symptom and Problem Index and the Pittsburgh Sleep Quality Index were completed.

RESULTS: Most were from the United States, between 56-60 years old and post-menopausal. Also they were predominantly Caucasian and had received a diagnosis of IC at least 10 years ago. Just under half self reported that they were depressed.

Mean global PSQI was 13.4 (SD± 3.64), with 100% of subjects scoring above 5. Results from the linear multiple regression analysis revealed that the predictor variables, nocturia, pain and urgency, were significant predictors of sleep quality, when controlling for age, depression, years with IC and menstrual status ($R^2 = 0.21, p < 0.001$). The specific symptoms of IC with the largest relationship with sleep quality were nocturia ($r = 0.427, p < 0.001$) and pain ($r = 0.411, p < 0.001$).

CONCLUSION: Women with IC have demonstrated poor sleep quality. Nocturia, pain, and urinary urgency contribute 21% of the variance for sleep quality.
CHAPTER 1: INTRODUCTION

Interstitial Cystitis (IC) is a chronic debilitating bladder condition that can affect people of any age, race, or sex (Dell, 2007; Parsons, Kurth, & Sant, 2007). The primary symptoms include pain, urinary frequency and urgency, and nocturia (Ito, Ueda, Honma, & Takei, 2007). The only definitive risk factor for IC is female gender, with the female to male prevalence ratio generally reported at 9:1 (Ibrahim, Diokno, Killinger, Carrico, & Peters, 2007).

Approximately 1.2 million women in the United States, are affected with IC. Although the number of people is relatively small, the severity of the symptoms and the chronic nature of this disease have tremendous impact on individual patients and their families (Parsons, et al., 2007). “The hardship of IC... (nerve pain, urinary burning, frequency, and urgency), controls lives and causes deep limitations on the individual’s lifestyle and severe sleep deprivation” (G Watkins, personal communication, December 17, 2008). Less than 50% of people with IC are able to work full time. Approximately 25% of patients are less than 30 years old when they first develop symptoms, but it generally takes four to seven years and numerous visits to multiple physicians to be diagnosed (Dell, 2007; Ibrahim, et al., 2007). Although the pain from this condition stems from the bladder, some women even undergo hysterectomies in a mistaken effort to
relieve the chronic pelvic pain (Dell, 2007; Ho, Koziol, & Parsons, 1997). Interstitial cystitis patients suffer in many ways due to their illness. One of the ways people with IC suffer is through its affects on sleep.

Sleep is an essential part of life because it contributes significantly to the restoration and recuperation of physical and mental functioning (Chartier-Kastler & Davidson, 2007). A number of studies have shown that even very brief periods of arousal from sleep can reduce its restorative power (Drake, Flynn, Romero, Weidner, & Amundsen, 2005; Freedman & Roehrs, 2007; Sayar, Arikan, & Yontem, 2002). Many medical conditions can cause these awakenings, leading to significant disturbances in sleep. Numerous negative effects of poor sleep quality have been documented in the research; including excessive daytime sleepiness, loss of productivity at work, heightened sensitivity to pain, depressive symptoms, increased stress, and a poorer quality of life (Asplund, 2004; Koblet, Borgstrom, & Mattiasson, 2003; Marin, Cyhan, & Miklos, 2006; Menefee, et al., 2000; Schneider & Stanley, 2007; Stewart, et al., 2003). Although IC patients may complain of sleep disturbances, the importance of sleep is often overlooked by most primary care providers. Patients are infrequently asked about their sleep quality and they do not always volunteer the information (Sigurdson & Ayars, 2007). If a sleep problem is identified, it is likely to be made light of and disregarded because the
practitioner thinks it is related to typical IC symptoms occurring during the night, and nothing further is done. Furthermore, discussion of disrupted sleep is notably absent within the IC literature.

The primary objective of this study is to first identify the frequency of disrupted sleep in individuals with interstitial cystitis and then to examine the relationship between poor sleep quality and IC symptoms, including urinary frequency, urgency, nocturia, and pain. The central hypothesis is that overall sleep quality is related to intensity or severity of IC symptoms. The goal is to provide a scientific base for evaluation and treatment of sleep difficulties in this population.

The Specific Aims of this study are as follows:

**Aim 1. Describe the frequency of disrupted sleep in women diagnosed with IC.**

Hypothesis 1: Patients with interstitial cystitis have disrupted sleep.

**Aim 2: Evaluate the relationship of disrupted sleep to specific IC symptoms.**

Hypothesis 2: The four symptoms (pain, urinary frequency, urgency, and nocturia) contribute to the variance of sleep quality.

Using the Pittsburgh Sleep Quality Index (PSQI) and O’Leary Sant Interstitial Cystitis Symptom and Problem Index, this study employed a cross-
sectional, descriptive, correlational research design. Participation in this study was offered to potential subjects online through a web-based peer support group for patients with IC. This study is innovative in that it characterized the relationships among IC symptoms and described the relative contributions of each IC symptom to sleep quality in women living with IC. The findings of this study begin to lay the scientific basis for interventions to help women with IC deal with the effects of disrupted sleep.
CHAPTER 2: BACKGROUND AND SIGNIFICANCE

Sleep is an essential part of life because it contributes significantly to the restoration and recuperation of physical and mental functioning (Chartier-Kastler & Davidson, 2007). A number of studies have shown that very brief periods of arousal from sleep reduce its restorative power. Many medical conditions can cause awakenings leading to significant sleep disturbances (Drake, et al., 2005; Freedman & Roehrs, 2007; Sayar, et al., 2002). Interstitial cystitis (IC) is a chronic debilitating condition of the bladder that can affect people of any age, race, or sex (Parsons, et al., 2007). Sleep disruption due to symptoms of pain, nocturia, or the sensation of need to void during the night are common complaints of IC patients in clinical practice. However, the discussion of disrupted sleep is notably absent within the IC literature. This lack of information leads to confusion and inconsistencies in the treatment of sleep disturbances in IC patients.

Sleep

Sleep is defined as a reversible unconscious state with characteristic supine sleep posture, lack of mobility, closed eyes, and increased arousal threshold. It is a time based cumulative process that can be impeded by several types of deprivation and also by systematic disturbances (Dement, 2005). Disrupted sleep can refer to a broad range of sleep-related problems, including
not getting enough sleep or sleep that is of poor quality and non restorative. According to the conceptual framework of the American Sleep Disorder Association criteria, arousals are the marker of sleep disruption representing a detrimental and harmful feature of sleep. This pattern of interrupted sleep is known as sleep disruption or fragmentation. An arousal is defined as a three second or longer shift towards awake (stage one sleep) noted in EEG frequency (American Academy of Sleep Medicine, 2005). Sleep disruptions can negatively affect many aspects of a person’s life.

Interest in sleep has existed since the dawn of history. Some of the world’s greatest thinkers, such as Aristotle, Hippocrates, Freud and Pavlov have attempted to explain the physiologic and psychological bases for sleep (Dement, 2005). Robert MacNish (1834) in The Philosophy of Sleep, wrote “Sleep is the intermediate state between wakefulness and death; wakefulness being regarded as that active state of all the animal and intellectual functions, and death as that of their total suspension” (p. 86). At that time sleep was universally regarded as an inactive state of the brain. In J. Allan Hobson’s book Sleep (1989) he states that “more has been learned about sleep in the past 60 years than in the preceding 6,000 years...” (p. 37). In this short period of time researchers have discovered that sleep is a dynamic behavior. “ Not simply the absence of waking, sleep is a special activity of the brain, controlled by
elaborate and precise mechanisms” (Hobson, 1989, p. 37) The contrast in these two statements about how sleep is perceived demonstrates a historical shift in sleep research and medicine from sleep as a passive process to sleep as an active process (Dement, 2005).

The idea that sleep is necessary to combat an illness was noted by Hippocrates and others. Getting extra and/or more restful sleep is considered conventional wisdom on fighting colds, fever, and other illnesses. Florence Nightingale in Notes on Nursing mentions that sleep is “all important” to the sick (Nightingale, 1860).

Medical conditions can increase normal awakenings, causing significant sleep disturbances (Drake, et al., 2005; Freedman & Roehrs, 2007; Sayar, et al., 2002). Even very brief arousals, if frequent, can decrease sleep’s restorative qualities (Freedman & Roehrs, 2007). This occurs because patients suffer from a lack of deep and rapid eye movement (REM) sleep. Chronic medical conditions such as fibromyalgia, chronic pain, and arthritis cause disrupted sleep, poor sleep quality, and lower quality of life scores (Marin, et al., 2006; Menefee, et al., 2000; Schneider & Stanley, 2007).

The effects of poor sleep quality are numerous and result in more than just excessive daytime sleepiness (Nugent, et al., 2001). Besides loss of sleep quality, disrupted sleep has been associated with loss of productivity at work
(Ekstedt, et al., 2006; Koblet, et al., 2003), depressive symptoms (Bixler, et al., 2005; Carney, Edinger, Manber, Garson, & Segal, 2007; Freedman & Roehrs, 2007; Goyal, Gay, & Lee, 2007), greater stress (Hamilton, Catley, & Karlson, 2007), a poorer quality of life (Chartier-Kastler & Davidson, 2007; Menefee, et al., 2000; Vena, Parker, Allen, & Bliwise, 2006). Additionally, cognitive and performance dysfunctions associated with sleep loss have been documented (Cote, Milner, Osip, Ray, & Baxter, 2003; Koblet, et al., 2003; Laurenson, 2003; Maher, Rego, & Asnis, 2006; Murray & Dodds, 2003). Furthermore, poor sleep can exacerbate certain disease symptoms. The lack of full cycle sleep or un-refreshing sleep can lower the pain threshold resulting in more severe pain. The increased pain results in lack of full cycle or un-refreshed sleep (Roehrs, Hyde, Blaisdell, Greenwald, & Roth, 2006).

Sleep and Women

Because IC primarily affects women, it is important to note that even healthy women are at greater risk for sleep problems, as demonstrated in the National Sleep Foundation’s (NSF) *Sleep in America* polls that examined sleep patterns of adult women (ages 18-64). In the 2000 study one in four women reported that pain or physical discomfort interrupted her sleep three nights a week or more. Pain conditions like migraines, tension headaches, rheumatic and arthritis conditions and heartburn are all more common among women.
Pain makes it harder to fall asleep or can lead to nighttime or early morning awakenings. Chronic pain is more frequently reported by women, at approximately double the rate in men (National Sleep Foundation, 2000). A linear relationship exists between pain and sleep. Pain can precede poor sleep complaints or occur subsequent to the pain; between 50%-90% of women with chronic pain complain of poor sleep (Armitage, Baker, & Parry, 2005).

The 2005 NSF *Sleep in America* poll revealed that women are more likely than men to have difficulty falling and staying asleep and to experience more daytime sleepiness at least a few nights/days a week (National Sleep Foundation, 2005). The female reproductive hormones, estrogen and progesterone, not only regulate reproductive tissue function during the menstrual cycle, but through their secondary actions in the central nervous system these hormones also influence sleep and circadian rhythms (Armitage, et al., 2005). Circadian rhythms, hormone secretion, body temperature, and sleep-wake activity are superimposed on the menstrual cycle rhythm. Women report more sleep disturbances during the premenstrual week than at other times (Shaver, 2002), with 33% of women reporting disturbed sleep during the week of their menstrual cycle (National Sleep Foundation, 2005).

According to the 2007 National Sleep Foundation *Sleep in America* poll, more women than men experience symptoms of insomnia at least a few nights
a week (67% vs. 54%) and they are more likely to have daytime sleepiness (National Sleep Foundation, 2007). Women of all ages are experiencing sleep problems, which change and increase in severity as they move through the different biological stages of their lives (Armitage, et al., 2005). Nightmares are reported more often by females then by males at any age (Armitage, et al., 2005). Additionally, 34% of women report experiencing a sleep disorder such as snoring, sleep apnea or restless leg syndrome. These sleep problems can led to daytime sleepiness, mood swings, anxiety and depression (National Sleep Foundation, 2007).

As described above women may have issues that result in poor sleep. Factors such as age, hormonal status, and mood (Moline, Broch, Zak, & Gross, 2003) are important variables to consider when studying women and sleep, as they can contribute to poor sleep.

Urologic Conditions and Sleep

Urologic conditions, particularly nocturia, cause disrupted sleep. Although voiding once at night is usually considered to be within normal limits, two or more voids at night can be disruptive to sleep and should be considered pathologic (Stewart et al., 2003). The International Continence Society defines ‘nocturia’ as “the complaint that the individual has to wake at night one time or more times to void” (Abrams, Cardozo, & Fall, 2002, p. 168).
This current definition of nocturia is not restricted to any particular number of nocturnal voids (Schneider & Stanley, 2007). Nocturia is usually caused by underlying pathophysiologic disorders including overactive bladder (OAB), pregnancy, medications, and conditions specific to men. These conditions may present separately or in combination.

In one study of 368 subjects, 73% of men and 57% of women reported that nocturia was their reason for unwanted early waking (Cole & Richards, 2007). Middle aged women, 40-60 years old, with nocturia had subjectively worse sleep maintenance (i.e. the ability either to sleep without waking up during the night or return to sleep quickly after waking) that was closely associated with an increased number of nocturnal voids. Women with three or more episodes of nocturia per night reported lower subjective health scores, increased frequency of physicians’ visits, increased use of hypnotics and a threefold increase in excessive daytime sleepiness (Chasens & Umlauf, 2003). Asplund (2004) reported that nocturia is strongly associated with sleep disturbances and a lower quality of sleep. Drake and colleagues (2005) studied 55 white women (32-89) and reported the risk of nocturnal polyuria increased with age beginning at 65 years. All the women were bothered by their nocturia as indicated by scores on urinary distress inventory, nocturia distress visual log, sleepiness scores, and insomnia scores.
Over 4,000 Danes aged 60-80 completed surveys which included the Nocturnal Enuresis and Sleep Interruption Questionnaire (NNES-Q), the Basic Nordic Sleep Questionnaire, and the Epworth Sleepiness Scale. Overall prevalence of nocturia was 75% for women and 78% for men, with no significant difference in gender. Age, however, did demonstrate an effect. A significantly higher number of nocturnal voids were associated with age, with 50% more voids occurring in the oldest group as compared with the youngest group. The median bother score, assessed by the NNES-Q, increased with the advancing number of nocturnal voids in both men and women (Bing et al., 2006).

Work impairment has also been reported due to a reduced productivity (N= 127) as a result of nocturia; 13% in the nocturia group reported impairment vs. 8.6% in the control group (p < 0.001). (Koblet, et al., 2003).

Overactive bladder is another urologic condition that causes urinary frequency and urgency and has been correlated with sleep disturbances. In people with an overactive bladder (OAB), the layered, smooth muscle that surrounds the bladder contracts spastically, sometimes without a known cause, which results in sustained high bladder pressure and the urgent need to urinate (Sand & Appell, 2006). The National Overactive Bladder Evaluation program was initiated to better understand the prevalence and burden of overactive
bladder. This survey (N=5,204) found that the overall prevalence was similar in men (16%) and women (16.9%). In women, the prevalence of OAB with urge incontinence increased with age from 2% (<60) to 19% (>60); in men it increased 0.3% (<60) to 8.9% (>60). OAB was associated with lower quality of life scores (as measured by the Short Form-36), higher Center for Epidemiologic Studies Depression Scale scores, and poorer quality of sleep. According to the results of the Medical Outcomes Sleep Scale women with overactive bladder accompanied by urge incontinence had a poorer quality of sleep than aged matched controls (mean 38.6 vs. 26.4, p < 0.001) (Stewart, et al., 2003).

The impact of OAB was documented by Coyne and colleagues (2008) in 1434 OAB cases matched by age, gender and country to 1433 controls. Among the people with OAB, 11.4% reported CES-D scores >21, compared to 3.6 % of controls (p < 0.001). Among participants less than 65 years old, rates of unemployment were higher for cases than controls (42.0% vs. 33.6%, p <0.001). OAB cases also had a greater impairment on two of three scales of the Work Productivity Related to Specific Health Problem Survey, with significant differences in percentage impairment at work due to health and percent of overall work impairment due to health (both p < 0.01). Almost a quarter of people who were less than 65 years old reported some sort of work impairment, as opposed to 12.2% of controls (p < 0.001). Cases reported slightly lower mean
EuroQoL-5D scores indicating lower overall health \((p < 0.001)\) Finally cases were less likely to report being sexually active in the past month \((62.4\% \text{ of cases vs. } 68.2\% \text{ of controls}; p = 0.002)\) and more likely to report decreased enjoyment of sexual activity \((15.4\% \text{ vs. } 2.8\% \text{ respectively, } p < 0.001)\). Thus, accumulating evidence shows that nocturia is associated with sleep disturbances and poor quality of sleep and quality of life.

**Interstitial Cystitis**

In order to understand the relationship between sleep disruption and IC symptoms it is necessary to understand the complexity of IC symptoms. IC is defined as pelvic pain, pressure, or discomfort related to the bladder, typically associated with persistent urge to void or urinary frequency, in the absence of infection or other pathology \((\text{Sant, Kempuraj, Marchand, } \& \text{ Theoharides, 2007})\). IC frequently goes undiagnosed and even misdiagnosed because it has no clear etiology or pathophysiology and therefore undefined diagnostic criteria \((\text{Panzera, 2007})\). Thus, the exact number of people with IC is unknown. It has been estimated to affect as many as 2 million people in the United States, with the mean age at onset of symptoms of 40 years. This condition poses a problem mostly for women \((9:1 \text{ female to male ratio})\), and being female is the only definitive risk factor \((\text{Butrick, 2007; Dell, 2007; Evans } \& \text{ Sant, 2007; Ibrahim, et})\).
al., 2007; Moldwin, Evans, Stanford, & Rosenberg, 2007; Steele & McLennan, 2007).

Normally, the lining of the bladder (epithelium) is protected from toxins in the urine by a coating of enzymes (mucopolysaccharides) called the glycoaminoglycan (GAG) layer. However, in IC, this protective layer is defective, allowing toxins to penetrate into the interstitial layers of the bladder wall, depolarize the nerve endings located there, and cause severe irritative voiding symptoms and bladder pain. The exact pathophysiology of IC is unknown; however, it is most likely multi-factorial. It is believed that defects in the bladder allow urine contents, such as potassium, to leak into the bladder lining, which may lead to mast cell activation and the release of histamine. These events may in turn, activate nerves, cause immunogenic and allergic responses, and lead to progressive bladder injury and chronic nerve pain. (Hurst, Moldwin, & Mulholland, 2007; Nazif, Teichman, & Gebhart, 2007; Sant, et al., 2007)

The first recognized case of IC could date from the mid 1800s. The first reliably documented case of interstitial cystitis was published in 1836 by Mercier. The term "interstitial cystitis" was first used in 1887 by Skene in his book *Diseases of the Bladder and Urethra in Women* (Samuals, 2005). Even after 150 years, there is still very little known about the illness--IC was not officially
recognized as a bladder disorder until about 20 years ago. Because physicians could find no organic cause, the prevailing medical opinion was that IC was a "hysterical female condition". Even Campbell’s Urology, the definitive text of urologic diseases, stated as late as 1986 that IC was "daunting in its evasion of being understood. [It] may represent the end stage of a bladder that has been made irritable by emotional disturbance" (p. 701). The book further states that interstitial cystitis may be a pathway for the discharge of unconscious hatreds. Today, IC is accepted as one of the most challenging conditions known to the urology community.

Although the number of affected people is relatively small, the severity of the symptoms and the chronic nature of this disease have tremendous impact (Rosenberg, Newman, & Page, 2007). The quality of life of IC patients is worse than patients experiencing chronic renal failure and undergoing dialysis (Ho, et al., 1997). Less than 50% of people with IC are able to work full time and 60% of IC patients have dysparunia significant enough to interfere with relationships. Women with IC are three to four times more likely to have suicidal ideations then the general public and five times more likely to have been treated for emotional problems. The increase in emotional problems may be related to the fact it can take four to seven years to receive a diagnosis, with patients seeing at least five physicians before they are diagnosed (Dell, 2007).
Approximately 25% of patients are less than 30 years old when they first develop symptoms (Ibrahim, et al., 2007). Some women even undergo hysterectomies for the chronic pelvic pain. But hysterectomy does not resolve their pain because the pain stems from the bladder (Butrick, 2007). Thus effects of IC are devastating.

IC symptoms are characterized by several motor and sensory dysfunctions of the bladder (Panzera, 2007). The primary symptoms of IC include the presence of abnormal urinary sensory urgency, pain with bladder filling, and feeling of need to urinate immediately which may or may not be accompanied by pain, pressure, or spasm of the bladder (Van de Merwe, 2007). This sensation of urgency leads to urinary frequency. The average number of voids for IC patients is 16 per day, twice the normal number (Rosenberg, Page, & Hazzard, 2007). Nocturia frequently accompanies the daytime urinary frequency and tends to increase as the severity of IC symptoms increase. Patients may also report pain over the supra-pubic area or referred pain located in the vagina, perineum, low back, or in the medial aspects of the thighs (Ottem, Carr, Perks, Lee, & Teichman, 2007). Symptoms of IC have a pattern of exacerbations and spontaneous remissions; these exacerbations are often referred to as flares. Symptoms of a flare initially presents with a sub-acute onset. Next, a rapid peak in symptom severity occurs, followed by a plateau
phase. Causes of flares include sexual intercourse, fluctuations in estrogen levels, allergies, physical or emotional stress, and diet (O'Leary & Sant, 1997). Patients with IC who are deprived of sleep because of their symptoms of IC may be at an increased risk for developing worsening IC symptoms. The increased pain, urinary urgency and frequency in turn, may indeed cause more sleep disruptions, leading to a continuous cycle of worsening IC symptoms and worsening sleep disruptions. Chronic pain and urinary frequency are hallmarks of IC. While chronic pain, as well as nocturia, has been documented to cause disrupted sleep in other medical conditions, research has not looked at sleep disruption in IC patients. In IC patients the importance of sleep is often unaddressed. Patients are infrequently asked about their quality of sleep and they do not always volunteer the information about sleep problems (Sigurdson & Ayars, 2007). When a sleep problem is identified, it is thought to be related to urinary frequency or pain that occurs during the night. Treatment options are focused on minimizing the overall frequency and pain for the patient. Unfortunately this does not always correct the problem, leaving patients to contend with the disrupted sleep on their own.

Although the exact interaction between sleep disruption and coexisting health problems is not always clear, the cycle of non-restorative nighttime sleep and impaired daytime mental and physical functioning is known to affect the
quality of a person’s life and work performance (Menefee, et al., 2000; Sigurdson & Ayars, 2007; Stewart, et al., 2003). Sleep disruptions can even cause certain medical conditions to worsen or not improve (Stewart, et al., 2003).

The Two Process Model of Sleep Regulation

A widely recognized model to explain sleep is Borbély’s (1982) two process model of sleep regulation (See Figure 1). According to this model, the timing and structure of sleep are determined by the interaction of a homeostatic and a circadian process. Homeostasis (process S) and circadian rhythmicity (process C) interact, influencing sleeping and waking. Process S (homeostatic drive for sleep) is a measure of sleep need and depends on the prior pattern of sleeping and waking. Process C (circadian control) is a sinusoidal rhythm with a time period of approximately 24 hours that is independent of sleeping or waking. Process C fluctuates across the day and night and is driven by a clock-like mechanism, located in the suprachiasmatic nucleus of the brain. Although processes S and C are conceptually separate, they are not independent of each other. Sleep propensity, sleep structure and waking are regulated by a subtle and complex interaction between the two processes and are mediated by neuro-endocrine and thermoregulatory functions. Therefore, mechanisms or factors that oppose or enhance process S or C can significantly affect timing, duration, and structure of sleep (Borbély & Achermann, 2005)
According to Borbély’s model, when sleep is disrupted the homeostatic drive to sleep is unable to return to its baseline level, causing a misalignment in the sleep cycle. This misalignment causes an increase in drive for sleep within a shorter time and increased fatigue during normal hours of wakefulness. When disrupted sleep occurs in women with IC due to the symptoms of urinary frequency, urgency and pain, it may then lead, via a feedback loop, to both increasing IC symptoms and further disrupted sleep.

Summary

It is evident that sleep disruption is related to urologic conditions. Nocturia causes disrupted sleep (Asplund, 2004; Schneider & Stanley, 2007; Stewart et al., 2003) which leads to a decreased quality of sleep (Asplund, 2004; Schneider & Stanley, 2007; Stewart et al., 2003). As the symptoms of nocturia increase so does the degree of bother (Bing, et al., 2006). Sleep contributes significantly to the restoration and recuperation of physical and mental functioning (Chartier-Kastler & Davidson, 2007). For sleep to be restorative it must be deep and continuous. Urologic conditions cause increased sleep disturbances (Asplund, 2004; Schneider & Stanley, 2007; Stewart et al., 2003) and decreased quality of sleep (Asplund, 2004; Schneider & Stanley, 2007; Stewart et al., 2003; Marin et al., 2006). Increased anxiety and depression in patients with disrupted sleep has also been described (Stewart et al., 2003).
Disrupted sleep and decreased sleep quality have been associated with a loss of productivity at work due to reduced sleep quality (Koblet et al., 2006; Menefee et al., 2000). Likewise, a poor night’s sleep can exacerbate certain disease symptoms such as pain and increased anxiety and depression (Stewart, et al., 2003).

Urology conditions have been shown to cause disrupted sleep, a lower quality of sleep and poorer function. While these findings have been demonstrated in nocturia and OAB it is not possible to draw conclusions based on this information regarding the effects of sleep in IC. Clearly there is a gap in the literature as there is no research on sleep quality in IC. This study will make a significant contribution to the IC literature, as it is the first of its kind to evaluate sleep quality and how sleep correlates with IC symptoms. By evaluating this relationship, it may be possible for a new treatment algorithm to be developed, thereby allowing providers to manage IC patient’s symptoms.
CHAPTER 3: METHODS

The purpose of this study was to first identify the frequency of disrupted sleep in women with interstitial cystitis and then to examine the relationship between poor sleep quality, and IC symptoms of urinary frequency, urgency, nocturia and pain. A multiple regression analysis was performed to quantify the severity and impact of IC symptoms and determine their impact on subjective sleep quality.

Design

This study was an anonymous web-based survey, employing a descriptive correlation design with cross-sectional data collection. This design is preferred because it is economical, there is a rapid turnaround in data collection, and it permits access to a larger pool of potential subjects. However, there are limitations which include convenience sample and self-selection

Recruitment and Selection of Subjects

Participants were recruited through the website of the Interstitial Cystitis Association (ICA). Formed in 1984, the ICA provides an international resource with the most up to date and accurate information on IC for both patients and healthcare providers. The ICA is dedicated to helping all those living with interstitial cystitis, as well as the healthcare providers and researchers who strive to improve the lives of IC patients. Individuals pay a nominal
membership fee the join the ICA. As of 2008, the ICA membership database consisted of over 10,000 people. The ICA provided access to their list-serve to notify members of this study. Subscribers received an e-mail regarding the study and asking for their participation (See Appendix 1). Within the e-mail potential participants were given a web page link which connected them to the study surveys. The survey was briefly described on the introductory page of the website. Data collection using rolling admission of a convenience sample took 12 days to achieve the desired sample size. Only participants who met the inclusion criteria were included in the study analysis.

**Inclusion Criteria**

- Female
- Read English
- Report diagnosis of IC diagnosis by potassium sensitivity test or bladder hydro-distension and/or bladder biopsy by a specialist
- Age 30 to 60 years

**Exclusion criteria**

- Male
- Does not read English
- Does not have a diagnosis of IC
• Under the age of 30 or above the age of 60

Sample Size Estimation

A power analysis was conducted to determine the sample size necessary to test the hypothesis. The sample size estimation for this study used the software program G*Power (Version 3.0.10, Dusseldorf, Germany). The power analysis was based on a linear multiple regression statistical analysis that assessed the relationship between the four symptom predictor variables (pain, urinary frequency, urgency, and nocturia) and the dependent/criterion variable (sleep quality). A study conducted by Freedman & Roehrs (2007) assessing the predictors for subjective sleep quality was used to estimate the effect size (Cohen’s $f$) for this study. An effect size is considered to be the smallest immediate effect that is clinically meaningful in the target population for the outcome measure, in this case sleep quality. The calculated value for the effect size was 0.07 which is a small effect (Cohen, 1988). For a significance level of alpha = 0.05 and to achieve a power of 0.80, a minimum sample of 176 subjects was required. Two hundred subjects were initially sought for this study to account for incorrect self selection regarding how the diagnosis of IC was made and by whom. After 200 women completed the study, review of the raw data indicated that over half the subjects reported depressive symptoms. In order to
control for this high prevalence of depressive symptoms, the projected sample size was increased to 700 subjects. The additional sample members were enrolled in 5 days.

Approval by Drexel University IRB was obtained before the recruitment of subjects. Addendum to the original application was submitted to increase the sample from 200 to 700 and it was approved. Due to a discrepancy in the definition of “participant” between QuestionPro and the Drexel University IRB, retroactive approval from the IRB was obtained to use all 877 participants.

Participants completed the investigator-developed demographic data form first. Next, they completed the O’Leary-Sant IC Symptom and Problem Index (O’Leary, Sant, Fowler, Whitmore, & Spolarich-Kroll, 1997) and Pittsburgh Sleep Quality Index. The entire process took approximately 10 minutes.

Measurements of Variables

Sleep Quality: Pittsburgh Sleep Quality Index (PSQI) is a self rated assessment of sleep quality and disturbances during the previous month. There are 19 individual questions which generate seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Individual questions are scored from 0 (not during the past month) to 3 (three or more
times a week). Each of the 7 components is calculated and scored from 0-3. The sum of scores for these seven components yields one global score which can range from 0 (good sleep) to 21 (very poor sleep). Global scores greater than 5 are indicative of sleep difficulty (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989). Acceptable measures of internal homogeneity, consistency and validity were obtained for the PSQI. The 7 component scores of the PSQI were evaluated for internal homogeneity and yielded an overall reliability coefficient (Cronbach’s alpha) of 0.83 A global PSQI score greater than 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% (kappa = 0.75, p < 0.001) in distinguishing good and poor sleepers (Refer to Appendix 2 for complete PSQI.) Reliability of this tool has been documented by other researchers between 0.70 and 0.80 (Dreher, 2003; Reishtein, 2005; Sayar, et al., 2002). In this study the Cronbach’s alpha was 0.75.

IC Symptom severity: O’Leary Sant IC Symptom and Problem Index is designed to measure the severity of symptoms and their impact on patients with IC. The questionnaire is comprised of 8 questions and 2 indices. The "symptom index" consists of 4 questions pertaining to the frequency of pain and urgency. The "problem index" includes 4 questions regarding the degree to which patients experience each symptom. Depending on the question, answers are assigned a score from 0 or 1 to 4, 5 or 6 as the maximum score. Summary
scores can range from 0 to 36 for both indices combined. Higher scores indicate more severe symptoms. Patients with IC typically score a total of 6 or more on each index. The Index has a Cronbach’s alpha of 0.85 for symptom index and 0.90 for the problem index. The test retest reliability is reported at 0.90 and 0.91 respectively. Both the Problem Index and the Symptom Index strongly discriminate IC patients from controls (O’Leary, et al., 1997). (See Appendix 3 for this instrument.) Other researchers have reported reliability of this tool as 0.70 - 0.85 (Nickel, Kaufman, Zhang, Wan, & Sand, 2007; Zhao, Bai, Zhou, & Du, 2008). In this study the Cronbach’s alpha was 0.83.

Other Covariates: Data was collected on socio-demographic variables, their IC illness and depressive symptoms, using an investigator-developed questionnaire. Socio-demographic variables include age, ethnicity, education, and income. Questions pertaining to IC were 1) number of years with diagnosis, 2) method of diagnosis, 3) type of specialist who made the diagnosis. Additionally, one question was added to assess menopausal status. (Demographic form may be found in Appendix 4.)

Depressive symptoms were measured using a single question: “Have you felt sad, down, depressed or blue almost every day of the past month? (This includes having little interest or pleasure in doing things)” (American Psychiatric Association, 2000; Furukawa, 1997; Hustey, 2005; Mitchell & Coyne,
2007). Data related to depressive symptoms were collected because of the potential confounding relationship between depression and sleep.

Procedure for Data Collection

Data collection for this study was conducted through an internet survey on www.Questionpro.com. As described above, members of the ICA were recruited through an e-mail that was generated through the ICA website. (See letter of support in Appendix 5.) According to our agreement, Ms Perilli forwarded the invitation to the members of the ICA via their list serve of active members. Included in this invitation was the web site link that connected potential participants to the Question Pro web site. Once the participants of the study connected to this secure web site, a brief description of the study including inclusion and exclusion criteria was displayed. Those willing to participate did so by continuing the on line survey hosted on QuestionPro servers. QuestionPro is a for profit company that hosts secured servers and exists to deliver the most advanced features that the online survey market demands while maintaining a balance between flexibility and ease-of-use (QuestionPro, 2008).

The process to utilize the web based survey host started with an agreement between the PI and QuestionPro and a professional account was
opened. The research questionnaires were manually entered by the PI in the “create survey” section of the web site. The PI duplicated the original questionnaires’ formats at closely as possible. For quality control the PI and Co-PI conducted a rehearsal of the survey process and data retrieval to ensure it was functioning properly prior sending the invitation e-mails. Responses were automatically collected and stored on QuestionPro’s private secure databases maintained in the United States. Upon completion of data collection the data was converted to an Excel spreadsheet by QuestionPro and downloaded to the PI’s personal computer. Additionally, a SPSS command file directly imported the data into SPSS for analysis.

Data Management and Analysis

The de-identified data were downloaded from QuestionPro and stored on the investigator’s personal computer. Security systems on that computer include MacAfee network firewall and virus protection technologies, password protected access, and a Dell biometric fingerprint scanner to ensure that only the PI could access the computer and data. The survey web site was also password protected. Only the PI and Co-PI had access to the passwords.

The data was analyzed using the Statistical Package for the Social Sciences Version 16 (SPSS, 2008). Cleaning of the data was conducted before all analysis, followed by identifying the characteristics of the sample. Frequency
distributions and measures of central tendency were conducted for all study variables. No outliers were found in this data set.

_Hypothesis 1: Patients with interstitial cystitis have disrupted sleep._ This hypothesis was tested using descriptive statistics, including means, medians and frequencies.

_Hypothesis 2: The four symptoms (pain, urinary frequency and urgency, nocturia) contribute to the variance of sleep quality._ Because the data for all variables were normally distributed, Pearson’s correlations were used to test how each IC symptom score was associated with the global PSQI score. Scatter plots of paired variables are displayed, with PSQI global on the y axis vs. predictor variables on the x axis. Based on statistical and theoretical significance, a hierarchical multiple regression analysis was conducted to determine the individual predictive contribution of each variable to the total variance in the PSQI. Assumptions as well as regression diagnostics were checked and were met prior to conducting the multiple regressions. Using linear multiple regression allowed for control of potential cofounders such as age, menstrual status, years with IC and depressive symptoms. Step one in the hierarchical regression added depressive symptoms. Step two included the entering of menstrual status. In step three age and years with IC diagnosis was added. Finally the symptom predictor variables (urinary urgency, frequency,
nocturia and pain) were entered in as a block. The multiple regression was repeated changing only the fourth step to enter the symptom predictor variables step wise. This was done to predict the individual contribution of each of the symptoms of IC. The data was then split case wise by dichotomous variables, depression and menstrual status. Finally, the data was split randomly and hierarchical multiple regression analyses were conducted on these split data sets. Using the “select cases at random” function in SPSS approximately 50% of the data was selected for cross-validation. Once the two random samples were selected the multiple regression analysis was run exactly like it was done on the initial model.

The SPSS syntax for all analyses may be found in Appendix 6.
CHAPTER 4: RESULTS

This chapter presents the study findings. The purpose of this study was to quantify sleep disruption in patients with IC and to evaluate the relationship of disrupted sleep to IC symptoms. Participants completed questionnaires including the PSQI to evaluate sleep quality, and the O’Leary Sant symptom and problem index to evaluate IC symptoms.

Data screening

Prior to conducting any statistical analysis, the data were screened to ensure completion, accuracy, and to test for normality of the distribution and the presence of outliers. Bi-variate correlation matrixes were used to estimate the correlation among pair-wise variables assessed in the study. Confounding variables were statistically controlled for in the analysis.

Sample

Recruitment of subjects took place over 12 days beginning November 26, 2008 and concluding on December 8, 2008. The recruitment e-mail was sent to approximately 10,000 ICA members; from that, 407 participants completed all items of the PSQI and O’Leary Sant surveys and were included in this study. (See figure 2 for sample enrollment flowchart.)
Figure 2

Sample Enrollment

1,544 people viewed the survey introduction

877 people began the survey

169 people dropped out mid survey

708 people completed the survey

22 people did not meet inclusion criteria

Leaving 686 total surveys

Minus 279 surveys, had one or more responses missing

407 surveys had all PSQI and O’Leary Sant questions
Demographic data

Most of the participants resided in the United States, between the ages of 56-60 years and were post-menopausal. They were predominantly Caucasian and had received at least a college education. They had received a diagnosis of IC at least 10 years ago. Just under half self reported that they were experiencing depressive symptoms. (See table 1 and figure 4.)

Statistical Description of the Variables

Table 2 presents the Mean (SD) and Table 3 shows the inter-correlation among the four predictor variables and their relationship with the criterion variable: global PSQI. Mean scores for the 4 symptom variables (urinary frequency, urgency, nocturia and pain) are moderately high (8.48 ± 2.3, 6.8 ± 2.8, 7.4 ± 2.6, 6.3 ± 2.1 respectively), reflecting a moderate to high degree of IC symptoms in this sample population.

A standardized scatter plot of the predictive variable by the residuals showed a random pattern across the entire range (Figure 9). Thus the assumption of homoscedasticity was met. No outliers were found in the data set. The data was verified to be normally distributed utilizing skewness and kurtosis values. Therefore two tailed Pearson r correlation coefficients were calculated between the extraneous variables (age, years since IC diagnosis, menstrual status, and depressive symptoms), the symptom predictors (urinary
urgency, frequency, nocturia and pain), and outcome variable (global PSQI score). (See Table 2.)

Reliability

The multi question instruments demonstrated acceptable internal reliability with a Cronbach’s alpha of 0.83 for the O’Leary Sant and 0.75 for the PSQI (Portney & Watkins, 2000).
Table 1
Demographics

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<th>frequency</th>
<th>percent</th>
</tr>
</thead>
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</tr>
<tr>
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<td>65</td>
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<td>36-40</td>
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<tr>
<td>menopausal</td>
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N=407
Table 2

Descriptive Statistics for Variables

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<td>21</td>
<td>13.12</td>
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N=407
Table 3

Pearson Correlations

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<th>Urge</th>
<th>Frequency</th>
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<th>Pain</th>
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</tr>
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<td>p*</td>
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<td></td>
<td>NS</td>
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<td>.000</td>
<td>NS</td>
<td>.000</td>
<td>.000</td>
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</tr>
<tr>
<td>Nocturia total sx&amp;prob</td>
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<td>.100</td>
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<td>.476</td>
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* two tailed significance

N=407
Figure 4
Participants by Geographic Location (N=407)
Hypotheses

Hypothesis 1 stated that patients with IC have disrupted sleep. This hypothesis was supported. The mean score of the global PSQI was 13.12 (SD ± 3.61) with all participants reporting a score of 6 or above. Scores 5 or above indicate poor subjective sleep quality.

Hypothesis two, the four symptoms of IC (pain, urinary frequency, urinary urgency, and nocturia) contribute to the variance of sleep quality was partially supported.

Results from the hierarchical multiple regression revealed that after controlling for age, menstrual status, years with IC, and depression, the four symptom predictors alone explained 21% of the variance, \(F(4, 398) = 8.41, p < 0.001\) in sleep quality. Only pain, nocturia, and urinary urgency contributed significantly \((p < 0.05)\) to the prediction model (see Table 4). Frequency was not a significant contributor to the prediction.

The multiple regression was conducted in a hierarchical manor. Depressive symptoms were added in step one. In step two, menstrual status was entered. At step three, age, and years with IC diagnosis were entered as a block. As the fourth and final step, the combined severity and impact scores for urinary frequency, urinary urgency, pain, and nocturia were added in as a block.
The results of the multiple regression analysis revealed that depressive symptoms explained 14% ($R^2 = 0.141$) of the variance in global PSQI scores. When menstrual status was entered in step two an additional 1% of the variance was explained ($R^2 = 0.153$) accounting for a total of 15%. Age and years with IC were added as step 3 and the total variance rose to 19%. Finally, in the last step the four symptom predictor variables were added in as a block, ordered as frequency, urgency, pain, and nocturia. The completed model explained 40% of the variance in sleep quality. Thus, after controlling for demographic variables, menses and depression, the symptoms of IC explained 21% of the variance in subjective sleep quality (Table 4).

The multiple regression was then repeated. Entering steps one, two and three as described above in the fourth step the symptom predictor variables were entered step wise. This process revealed nocturia contributed 16% ($R^2 = 0.157$) to the variance of sleep quality (Figure 6). When pain was entered it contributed an additional 4% ($R^2$ change = 0.041) (Figure 7). Urgency accounted for 1% ($R^2$ change = 0.013) (Figure 4). Once the other symptoms predictors were entered in the model, frequency was not a significant contributor to the variance of global sleep quality (Figure 5). Therefore, 21% of the variance in sleep quality can be explained by nocturia, pain, and urinary urgency (Table 5).
Leaving the predictor variable, nocturia, out of either model did not significantly change the contribution of pain on the variance of subjective sleep quality.

Hypothesis 2 was partially supported because urinary frequency did not contribute significantly to the variance of sleep quality.

Confirmatory analyses of the model were performed by splitting the data set based on dichotomous variables, depression and menstrual status. Hierarchical multiple regression analyses were run with the symptom predictor variables entered as a block.

In patients without depressive symptoms (N=228) the total adjusted $R^2 = 0.31$ ($p < 0.001$), indicating the model explained 31% of the variance. After controlling for age, menses and years with IC, the symptom predictor variables alone explained 29.5% of the variance in sleep quality ($R^2 = 0.295$). In patients with depressive symptoms (N = 179) the total model explained 20% of the variance ($R^2 = 0.196$, $p < 0.001$). Controlling for age, menses and years with IC the symptom predictor variables explained 17.1% of the variance ($R^2 = 0.171$, $p < 0.001$).

In menstruating women (N = 186) an $R^2$ of 0.354 ($p < 0.001$) was calculated indicating a 35% explanation in the variance. After controlling for age, years with IC and depression, 25.4% of the variance in sleep quality was explained by the
symptom predictor variables ($R^2 = 0.254$). The analysis of post-menopausal women ($N = 221$) revealed a 26% explanation ($R^2 = 0.264, p < 0.001$). However after controlling for confounding variables 14% ($R^2 = 0.14$) of the variance was explained by the symptoms of IC alone.

Finally, cross validation of the model was performed by randomly splitting the data set into two via SPSS. Hierarchical multiple regressions were run on the randomly selected data sets. The first step depression was added. In the second step menstrual status was added. Age and years with IC diagnosis were entered as a block in step three. Finally, the symptom predictor variables, severity and impact score for pain, urinary urgency, urinary frequency, and nocturia were added in a block. Utilizing this process, after controlling for age, menstrual status, years with IC, and depression, the symptom predictor variables explained 20% ($R^2 = 0.201, p < 0.001$) and 21 % ($R^2 = 0.211, p < 0.001$) of the variance in global PSQI scores.
Table 4

Model Summary for Total Sample

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<tr>
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<th>R Square Adjusted</th>
<th>Std. Error of the Estimate</th>
<th>R Square Change</th>
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<th>df2</th>
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a. Predictors: depression

b. Predictors: depression, menses

c. Predictors: depression, menses, IC years, age

d. Predictors: depression, menses, IC years, age, pain total, nocturia total, urge total, frequency total.

Dependent Variable: Global PSQI
Table 5

Model Summary for Total Model Stepwise

<table>
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<tr>
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<th>Adjusted R Square</th>
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</table>

a. Predictors: depression
b. Predictors: depression, menses
c. Predictors: depression, IC years, age
d. Predictors: depression, menses, IC years, age, nocturia
e. Predictors: depress, menses, IC years, age, nocturia, pain
f. Predictors: depress, menses, IC years, age, nocturia, pain, urgency

Dependent Variable: Global PSQI
Additional findings

Descriptive statistics were used to evaluate the degree of IC symptoms in the sample population. All of the symptom and impact scores were high. Urinary frequency led the symptoms in regards to overall mean (8.56 ± 2.3). However frequency was not a significant predictor of the variance of sleep quality in the total sample model. (See Table 4)

Urinary urgency and nocturia had lower means (6.91 ± 2.85, 7.43 ± 2.58, respectively) but both had modes at the maximum score 11, indicating a ceiling effect.

PSQI component scores

PSQI component scores were analyzed by descriptive statistics to determine the area which most impairment occurred. Habitual sleep efficiency scores had the highest mean (2.99), median (3) and mode (3). This means that the majority of participants spend large periods of time in bed not asleep. (Table 5)
Table 6

PSQI component score

<table>
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<th>Mean</th>
<th>Std. Deviation</th>
<th>Range</th>
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<tr>
<td>Sleep disturbances</td>
<td>1.76</td>
<td>0.62</td>
<td>3</td>
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<tr>
<td>Daytime function</td>
<td>1.7</td>
<td>0.86</td>
<td>3</td>
</tr>
<tr>
<td>Habitual sleep efficiency</td>
<td>2.99</td>
<td>0.13</td>
<td>3</td>
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</table>
Figure 4

Urinary Urgency Scatter Plot

R^2 Linear = 0.196
Figure 5

Urinary Frequency Scatter Plot
Figure 6

Nocturia Scatter Plot
Figure 7

Pain Scatter Plot
Figure 8

Scatter Plot for Homoscedasticity
CHAPTER 5: DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

This chapter will discuss the results of the study. The chapter begins with discussion of the research questions, research hypotheses, and other central findings. Additionally this chapter includes implications for nursing science, overall study conclusions, limitations, and recommendations for future studies.

The purpose of this study was to quantify disrupted sleep in women with IC, and to explore the relationships between the symptom predictor variables urinary frequency, urgency, nocturia and pain, with the outcome variable, subjective sleep quality.

Prior empirical research has demonstrated disrupted sleep and poor sleep quality in medical conditions that share symptoms experienced by women with IC, such as nocturia and OAB (Bing, et al., 2006; Drake, et al., 2005; Sand & Appell, 2006). Additionally, there is documentation of poor sleep quality in other chronic medical conditions. However this is the first study to look at sleep in this specific population.

Research Question and Research Hypotheses

The following hypotheses were tested in this study.

Hypothesis 1: Patients with interstitial cystitis have disrupted sleep

This was supported.
Hypothesis 2: The four symptoms (pain, urinary frequency, urgency, and nocturia) contribute to the variance of sleep quality.

This was partially supported. After controlling for extraneous variables urinary urgency, frequency and nocturia contributed significantly to the variance in sleep quality but frequency did not.

Conclusions

This convenience sample of women with IC exhibited poor subjective sleep quality. This agrees with earlier findings of poor sleep quality in conditions with symptoms similar to IC as well as in other chronic medical condition such as COPD, HIV, fibromyalgia, and chronic pain disorders. These conditions have reported global PSQI scores ranging from six to eleven (Dreher, 2003; Marty, et al., 2008; Menefee, et al., 2000; Reishtein, 2005; Sayar, et al., 2002; Theadom, Cropley, & Humphrey, 2007). This study found global PSQI scores (mean 13.3) were higher in the IC population than in other chronic medical conditions. This indicates very poor sleep quality, unique to the IC population.

Three of the four individual symptoms of IC demonstrated a significant relationship to poor sleep. These findings indicate that women with IC have a higher likelihood of reporting poor sleep due to nocturia, pain, and urgency and that a positive linear relationship exists between severity of IC symptoms and poor sleep. Nocturia, followed by pain, was the most significant predictor of
poor sleep quality. Interestingly the symptom with highest reported mean score, urinary frequency, was not a significant predictor of sleep quality in this model. Since frequency and nocturia had a moderate significant correlation ($r = 0.613$) the co-linearity relationship between them could explain this finding.

When the data was split based on the depression screening question, the model explained a higher percentage of variance in patients without depressive symptoms. After splitting the data based on menstrual status, the model was a better predictor for menstruating women. Therefore this model has a better predictive power in women without depression and in women who are still menstruating. This may be explained by the confounding effects depression and menopause have on sleep (Baker, Simpson, & Dawson, 1997; Carney, et al., 2007; Haynes, McQuaid, Ancoli-Israel, & Martin, 2006; Terashima, et al., 2004).

Additionally cross-validation of the model revealed symptom predictors explained the variance within 5% of the original model’s variance. This indicates that the model is capable of accurately predicting the same outcome from the same set of predictors in different groups of people.

Discussion

This study is the first to document sleep problems in women with IC. All of the participants had global PSQI score indicating poor subjective sleep quality. This is notably more prevalent than in other conditions. This finding was almost
universally experienced in IC. Twenty one percent of the variance in sleep quality can be explained by the symptoms of IC. This is important because poor sleep is associated with many co-morbid conditions.

There are many overlapping issues that affect sleep in this population. This sample reported a high prevalence of depressive symptoms. Most people with depression complain of insomnia, specific features of which include difficulty falling asleep, frequent awakenings at night, non restorative sleep, and decreased total sleep (Benca, 2005). People with insomnia lie in bed, awake, ruminating on not being able to sleep, which results in poor sleep efficiency (the ratio of time spent asleep [total sleep time] to the amount of time spent in bed) (Perlis, Smith, & Pigeon, 2005). This habit can lead to anxiety regarding sleep, in which the bed becomes associated with being awake instead of being associated with sleeping. Sleep efficiency can be subjectively identified on the PSQI, as in this study, or objectively by polysomnogram. Sleep efficiency was the highest component score of the PSQI in this sample, demonstrating that women with IC, like people with insomnia, spend a great deal of time in bed but not sleeping. This practice develops poor sleep hygiene routines which only perpetuate the process of lying in bed but not sleeping.

Borbély proposed that sleep is regulated by the interaction of two processes: a homeostatic, sleep-inducing process (process S), which rises
exponentially during wakefulness and declines exponentially during sleep, and a circadian process (process C), which reflects an internal clock that governs circadian propensity for sleep (Borbély, 1982). Borbély suggests that process S is deficient in patients with depression (Borbély & Wirz-Justice, 1982). Process S is considered to be an inhibitor of REM sleep; therefore, the less SWS (which reflects process S), the shorter the REM sleep latency, the longer the first REM sleep period, and the higher the REM sleep density (Benca, 2005).

Depression is a common finding in people with chronic pain. In general two out of three patients with chronic pain complain of poor sleep quality or an un-refreshing sleep. Chronic pain and sleep disturbances are more prevalent in women than in men and increase with age (Call-Schmidt & Richardson, 2003). Subjective sleep complaints in people with chronic pain are similar to those of insomnia and include difficulty falling asleep, early morning awakening, dissatisfaction with sleep quality or quantity, non-restorative sleep and daytime sleepiness or fatigue. Objective sleep abnormalities documented in chronic pain patients include increased sleep fragmentation and decreased sleep efficiency (Morphy, Dunn, Lewis, Boardman, & Croft, 2007; Ohayon, 2002). Studies have identified a significant temporal bi-directional relationship and reciprocal interactions between sleep quality and pain severity. While pain can cause poor sleep, poor sleep has been identified to increase pain sensation. A night of sleep
disturbances can predict next day pain (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996; Castillo, et al., 2006; Davies, et al., 2008; Edwards, Almeida, Klick, Haythornthwaite, & Smith, 2008; Morphy, et al., 2007; Raymond, Nielsen, Lavigne, Manzini, & Choiniere, 2001; Roehrs, et al., 2006; M. T. Smith, Edwards, McCann, & Haythornthwaite, 2007). Additionally REM sleep restriction, a result of frequent awakening, causes next day hyperalgesia (Roehrs, et al., 2006). This effect can be seen in women with IC because frequent nocturia or pain results in fragmented sleep which then will additionally decrease REM sleep. Lastly, women with IC are often treated with tricyclic anti-depressants, anti-cholinergic medications, anti-convulsants, and opioids, all of which have adverse effects on sleep (Bonafide, et al., 2008). All of these are known to suppress REM sleep and alter short wave sleep (Brown; DeMartinis, Winokur, DeMartinis, & Winokur, 2007; Pagel, 2005). Solving this problem is not a simple matter of increasing medications. Decreasing pain or controlling symptoms with opioids or other common medications used to manage IC symptoms, will alter sleep architecture and actually decreases the next day’s pain threshold (Roehrs, et al., 2006). This population has many contributors to sleep disturbances, which produce a cyclical negative process linking pain, depression, and sleep.

Interstitial cystitis patients have depression and chronic pain, both of which contribute to their poor sleep. Poor sleep can lead to insomnia and chronic
insomnia corresponds to low sleep efficiency, as indicated by the PSQI scores. Therefore, evaluating IC patients for insomnia and treating when appropriate may be beneficial.

The predictor variables in this model accounted for a 40% explanation of the variance, in subjective sleep quality. To improve the predictability of this model additional variables need to be added. Candidate variables include lifestyle, hormones, and obstructive sleep apnea.

Some of the unexplained variance of sleep quality may be associated with lifestyle. Interstitial cystitis predominately affects females who tend to be the caretakers of the family and household. Issues related to work, children, spouses, and aging parents, as well as stress and anxiety may be a factor in poor sleep quality. If they are tired from lack of sleep, they may increase caffeine usage which can lead to worsening sleep problems (Cheek, Shaver, & Lentz, 2004; Hamilton, et al., 2007; B. W. Smith & Zautra, 2008; M. T. Smith, et al., 2007).

Sleep problems, particularly disrupted sleep, are common in women during the menopause transition (Eichling & Sahni, 2005; Moe, 2005). These sleep problems are thought to be associated with hormonal function: the association of hot flashes with a shorter amount of total sleep time and a higher incidence of arousals from sleep (Freedman & Roehrs, 2007). Hot flashes that occur during sleep have the ability to affect the quality of sleep adversely by bringing women
from a deeper, more restful stage of sleep to a lighter, less restful and restorative stage, and even to a full awakening if the hot flash is followed by heavy sweating. Hot flashes before bed may also cause insomnia (Moe, 2004). Insomnia related to the menopause transition has also been attributed to increased depression or anxiety, which may affect the time it takes to fall asleep (Moe, 2005).

In premenopausal women, the incidence of sleep-disordered breathing is quite small (about 1%) but it increases dramatically (to 9%) after menopause (D’Ambrosio, Stachenfeld, Pisani, & Mohsenin, 2005; Pressman, Figueroa, Kendrick-Mohamed, Greenspon, & Peterson, 1996). Nocturia, a common symptom in a variety of medical disorders, is relatively common in OSA patients (Pressman, et al., 1996). Nocturia secondary to sleep disordered breathing would be causatively different from nocturia secondary to IC, and would require different diagnostic procedures and treatment (Chasens & Umlauf, 2003; Umlauf, et al., 2004).

Many similarities between these conditions remain to be explored in this population. It is clear however, that in a group with a mean age range of 56–60, of whom 54% of participants are menopausal, and 45% of whom self report depressive symptoms, that there is an overlap of conditions which can cause
poor sleep. Further research aimed at disentangling the exact cause and effect is crucial to the development of interventions for this population.

Specific Significance to Nursing Practice

IC symptoms are most often managed by nurses. Because there is not a cure for this condition, caring for the patient is sometimes all that can be done. Nurses are expert caregivers. Many of the strategies for symptom relief require behavior management techniques. Nurses excel in patient education and have the time and resources to assist patients in making these lifestyle changes. When IC patients are treated with pharmacologic agents, the regime is complex and improvement is slow at best. Therefore, careful teaching, maintenance and adjustments are often needed. These tasks are often the responsibility of the advanced practice nurse. Determination of the relationships of sleep and IC symptoms will allow nurses to focus on the most pressing sleep issues. Screening for particular symptoms, such as nocturia and pain and then managing these symptoms could lead to better sleep quality. Examining the area of largest impairment may help providers target their approach to optimal care to patient symptoms.

The elevation of sleep efficiency scores on the PSQI indicated that women with IC are spending time in bed while not sleeping. Nurses can utilize cognitive behavioral therapy for insomnia and educate and teach patients about sleep
hygiene to improve sleep quality. One of the first steps of CBT is to drastically limit the amount of time the person spends in bed, when she does get into bed, she is exhausted and can fall asleep almost immediately. Gradually the time in bed is lengthened, extending the time spent asleep (Edinger, Wohlgemuth, Krystal, & Rice, 2005; Manber, et al., 2008). Nurses should be aware that cause of the poor sleep quality can be multifactoral. Therefore appropriate screening of all conditions that may interfere with sleep in this population such as chronic insomnia, depression, and OSA should be performed.

Limitations

The limitations of this study are as follows: 1) sample selection bias, 2) use of self report measures, 3) response bias, and 4) large amount of missing data. Sample recruitment may have favored a population with more severe symptoms, who may be more likely to access the ICA web site in hopes of finding support, treatment options, and healthcare providers. The research findings may therefore not be applicable to the entire IC population. Additionally, this was an internet study and therefore it was limited to women who have access to a computer. Reliance on self report is a concern. Survey measures, like the ones used in this protocol, require participant recall to answer the question. Recall biases may cause answers to be noted as worse or better then they truly are. Data on subjective symptoms severity should ideally be collected at the time they are
experienced because recall of the severity of the symptoms may be inaccurate. Response bias may have also occurred. This is when respondents answer questions in the way they think the questioner wants them to answer rather than according to their truth. The large number of incomplete survey was also a limitation in this study. Epidemiology studies regarding IC report this as a condition that predominantly affects white women. However, given the number of physician visits it takes to obtain an accurate diagnosis, researchers could be missing the un-insured or under insured women with IC. Therefore a final issue is, is 95% white really the demographic picture of IC?

Implications for future nursing research

As this study was the first to look at sleep quality in women with IC, many issues remain to be investigated in the future. There is a strong association between sleep disturbances and depression (Benca, 2005). Therefore women with IC in this study may have underestimated or under reported their depressive symptoms. Use of a multi item tool to measure depression is indicated to more accurately measure this variable. Future studies should use a multi item tool for depression to better determine the correlations between these variables and sleep quality.

Pain is a complex issue and therefore a multidimensional tool for pain may be indicated in the future for better evaluation. Clarification regarding
specific menstrual status may also be beneficial. This could include asking participants to report their last normal menstrual period or can include serum LH and FSH levels. Sleep in men with IC is an area where a gap in the literature exists as well. Repeating this study in men would provide an interesting comparison. Additionally, the quantification of anxiety in this population would be beneficial. Screening for primary sleep disorders or other medical conditions that may interfere with sleep quality would also provide more thorough explanation of variance in sleep. Qualitative research with regards to sleep and IC will provide additional information regarding this area, especially for aspects which were not addressed in questionnaires. Using polysomnogram testing in people with IC would provide objective sleep quality data regarding this topic. All of this information can eventually lead to the development and then the testing of an intervention used to improve sleep.

Summary

Women with IC have disrupted sleep and poor subjective sleep quality. Predominant symptoms of IC related to poor sleep include nocturia and pain. Identifying these symptoms will aid nurses in screening for symptoms and raise awareness of poor sleep quality in this population of women. The cause of poor sleep quality in this population is multi-factorial therefore screening for insomnia, depression, and OSA should be performed when indicated. Additional
research is needed in this area to add to the body of literature and to develop and test intervention for women with IC and poor sleep.
References


Figure 1

A Two-Step Process of Sleep Regulation

Timecourse of sleep processes after regular and extended waking periods. Upper part: Exponential decline of slow wave activity over four consecutive sleep cycles (value of first cycle = 100%) for baseline night (continuous line) and after sleep deprivation (interrupted line). The exponential increase of slow wave sleep propensity during waking time is indicated by the dotted curve. Lower part: Timecourse of Process S and the negative function of Process C (curve C).

APPENDIX 1: Demographic Questions

Please answer the following questions.

1. How old are you?
   a. 30-35
   b. 36-40
   c. 41-45
   d. 46-50
   e. 51-55
   f. 56-60

2. Which best describes your race?
   a. White
   b. Black or African American
   c. Asian or Pacific Islander
   d. Hispanic or Latino
   e. Native Hawaiian or Other Pacific Islander
   f. American Indian or Alaska Native

3. Which best describes your level of education?
   a. High school graduate
   b. Some college courses
   c. College graduate
   d. Post-graduate courses
   e. Other

4. What is your religious background?
   a. Christian
   b. Buddhist
   c. Hindu
   d. Jewish
   e. Muslim
   f. Sikh
   g. Any Other Religion
   h. None
5. What is your annual household income?
   a. Under $15,000
   b. $15,000–$24,999
   c. $25,000–$34,999
   d. $35,000–$49,999
   e. $50,000–$74,999
   f. $75,000–$99,999
   g. $100,000 and over

6. How long have you had interstitial cystitis?
   a. Less than 1 year
   b. 1-2 years
   c. 3-5 years
   d. 6-10 years
   e. More than 10 years

7. How was your interstitial cystitis diagnosed?
   a. Questionnaire or Survey
   b. Potassium sensitivity test /bladder challenge (two solutions placed in the bladed and compared)
   c. Office cystoscopy (look inside the bladder)
   d. Cystoscopy with bladder hydro-distension (look inside the bladder under anesthesia in the hospital)
   e. Other
   f. I don’t know

8. Who diagnosed your interstitial cystitis?
   a. Medical or primary care provider
   b. Gynecology or women’s health specialist
   c. Urologist
   d. Uro-gynecologist

9. Over the past month have you been bothered by feeling sad, down, depressed or blue; or had little interest or pleasure in doing things?
   Yes   No
Dear Alis:

ICA Board Co-chair, Marianne Schuster, recently contacted you regarding your current IC study. She shared your emails with me and we discussed how the ICA could best serve your recruitment needs.

How does the following sound:

1. We can send out a blast email to the 10,000-plus IC patients in our database. The blast would direct them to you. Do you have, on your end, a website, email address, or telephone number dedicated to this project? This is vital for any type of patient recruitment.

2. We can also include your recruitment information in our monthly online news digest, Cafe ICA. The July issue of Cafe ICA is currently being posted on the site, so if we included the announcement in Cafe ICA, it would have to be the August issue which should be on our website at the end of August.

For either or both options, we would need you to provide us with the "official language" that you want to use to describe your project, recruiting, etc. And we would also need some place to direct the respondents so that they can directly access you.

Your research into IC, sleep, and depression sounds very interesting. Please let us know if the above ideas work for you.

Best regards,

Lucretia (Creda) Perilli

ICA Director of Medical Communications
APPENDIX 3: O’Leary Sant Interstitial Cystitis Symptom and Problem Index

During the past month how much has each of the following been a problem for you:

**Q1.** How often have you felt the strong need to urinate with little or no warning?

1. __ Not at all
2. __ Less than 1 time in 5
3. __ Less than half the time
4. __ About half the time
5. __ More than half the time

**Q2.** Have you had to urinate less than 2 hours after you finished urinating?

1. __ Not at all
2. __ Less than 1 time in 5
3. __ Less than half the time
4. __ About half the time
5. __ More than half the time

**Q3.** How often did you most typically get up at night to urinate?

1. __ None
2. __ Once
3. __ 2 times
4. __ 3 times
5. __ 4 times
6. __ 5 or more times

**Q4.** Have you experienced pain or burning in your bladder?

0. __ Not at all
1. __ A few times
2. __ Almost always
3. __ Fairly often
4. __ Usually
During the past month how much has each of the following been a problem for you:

**Q1.** Frequent urination during the day?
1. __ No problem
2. __ Very small problem
3. __ Small problem
4. __ Medium problem
5. __ Big problem

**Q2.** Getting up at night to urinate?
1. __ No problem
2. __ Very small problem
3. __ Small problem
4. __ Medium problem
5. __ Big problem

**Q3.** Need to urinate with little warning?
1. __ No problem
2. __ Very small problem
3. __ Small problem
4. __ Medium problem
5. __ Big problem

**Q4.** Burning, pain, discomfort, or pressure in your bladder?
1. __ No problem
2. __ Very small problem
3. __ Small problem
4. __ Medium problem
5. __ Big problem

APPENDIX 4: Pittsburgh Sleep Quality Index (PSQI)

Instructions:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.
Please answer all questions.

1. During the past month, when have you usually gone to bed at night?

USUAL BED TIME

2. During the past month, how long (in minutes) has it usually take you to fall asleep each night?

NUMBER OF MINUTES

3. During the past month, when have you usually gotten up in the morning?

USUAL GETTING UP TIME

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

HOURS OF SLEEP PER NIGHT

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

(a) Cannot get to sleep within 30 minutes

| Not during the past month | Less than once a week | Once or twice a week | Three or more times a week |
(b) Wake up in the middle of the night or early morning

<table>
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<tr>
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<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
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</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
<td></td>
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</tbody>
</table>

(c) Have to get up to use the bathroom

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<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
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<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
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(d) Cannot breathe comfortably

<table>
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<th></th>
<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(e) Cough or snore loudly

<table>
<thead>
<tr>
<th></th>
<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
<td></td>
<td></td>
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</table>

(f) Feel too cold

<table>
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<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

(g) Feel too hot

<table>
<thead>
<tr>
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<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(h) Had bad dreams

<table>
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<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(i) Have pain

Not during the past month  Less than once a week  Once or twice a week  Three or more times a week

(j) Other reason(s), please describe ________________________________

How often during the past month have you had trouble sleeping because of this?

Not during the past month  Less than once a week  Once or twice a week  Three or more times a week

6. During the past month, how would you rate your sleep quality overall?

Very good
Fairly good
Fairly bad
Very bad

7. During the past month, how often have you taken medicine (prescribed or “over the counter”) to help you sleep?

Not during the past month  Less than once a week  Once or twice a week  Three or more times a week

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month  Less than once a week  Once or twice a week  Three or more times a week
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all
Only a very slight problem
Somewhat of a problem
A very big problem

APPENDIX 5: Recruitment Ad

Sleep and Interstitial Cystitis Symptoms

A doctoral student in nursing is asking for your participation in an innovative study looking at sleep quality and interstitial cystitis symptoms. This 20 minute on-line questionnaire that is voluntary and completely confidential. You will be asked to complete several questions about your interstitial cystitis symptoms; your sleep habits; and some demographic information.

If you are: 1. Between the age of 30-60 years old

2. And have a diagnosis of interstitial cystitis made by a specialist who performed a potassium sensitivity test or bladder hydro-distension

You qualify to be part of this study. To find out more, or to participate in this study click on the following link.
APPENDIX 6: SPSS Syntax

GET

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DATASET NAME DataSet1 WINDOW=FRONT.

REGRESSION

/MISSING LISTWISE

/STATISTICS COEFF OUTS R ANOVA

/CRITERIA=PIN(.05) POUT(.10)

/NOORIGIN

/DEPENDENT GlobalPSQI

/METHOD=ENTER Urgency Frequency Nocturia Pain_IC

/SCATTERPLOT=(*ZPRED,*ZRESID).

FREQUENCIES VARIABLES=age ICyears depress menses_regress race

/STATISTICS=STDDEV VARIANCE RANGE MINIMUM MAXIMUM SEMEAN MEAN MEDIAN MODE SKEWNESS SESKEW KURTOSIS SEKURT

/ORDER=ANALYSIS.

FREQUENCIES VARIABLES=Urgency Frequency Nocturia Pain_IC GlobalPSQI
/STATISTICS=STDDEV VARIANCE RANGE MINIMUM MAXIMUM SEMEAN MEAN MEDIAN MODE SKEWNESS SESKEW KURTOSIS SEKURT

/ORDER=ANALYSIS.

GET

FILE='C:\Users\Alis\Documents\SPSS\sleep_and_IC_complete_revised_with_5J.sav'.

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CORRELATIONS

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/PRINT=TWOTAIL NOSIG

/STATISTICS DESCRIPTIVES

/MISSING=PAIRWISE.

DATASET ACTIVATE DataSet2.

DATASET CLOSE DataSet1.

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>Error # 63 in column 8. Text:
C: \ Users \ Alis \ Documents \ SPSS \ complete_data_set

> The file does not exist.

> This command not executed.

DATASET NAME DataSet1 WINDOW=FRONT.

CORRELATIONS

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/PRINT=TWOTAIL NOSIG

/STATISTICS DESCRIPTIVES

/MISSING=PAIRWISE.

GRAPH

/SCATTERPLOT(BIVAR)=GlobalPSQI WITH Urgency

/MISSING=LISTWISE.

GRAPH

/SCATTERPLOT(BIVAR)=GlobalPSQI WITH Frequency

/MISSING=LISTWISE.
GRAPH
/SCATTERPLOT(BIVAR)=GlobalPSQI WITH Nocturia
/MISSING=LISTWISE.

GRAPH
/SCATTERPLOT(BIVAR)=GlobalPSQI WITH Pain_IC
/MISSING=LISTWISE.

REGRESSION
/DESCRIPTIVES MEAN STDDEV CORR SIG N
/MISSING LISTWISE
/STATISTICS COEFF OUTS CI BCOV R ANOVA COLLIN TOL CHANGE ZPP
/CRITERIA=PIN(.05) POUT(.10)
/NOORIGIN
/DEPENDENT GlobalPSQI
/METHOD=ENTER depress
/METHOD=ENTER menses_regress
/METHOD=ENTER age ICyears
/METHOD=STEPWISE Urgency Frequency Nocturia Pain_IC
/SCATTERPLOT=(*ZPRED,*ZRESID)
/RESIDUALS HIST(ZRESID) NORM(ZRESID).
REGRESSION

/DESCRIPTIVES MEAN STDDEV CORR SIG N

/MISSING LISTWISE

/STATISTICS COEFF OUTS CI BCOV R ANOVA COLLIN TOL CHANGE ZPP

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/NOORIGIN

/DEPENDENT GlobalPSQI

/METHOD=ENTER depress

/METHOD=ENTER menses_regress

/METHOD=ENTER age ICyears

/METHOD=STEPWISE Urgency Frequency Nocturia Pain_IC

/SCATTERPLOT=(*ZPRED,*ZRESID)

/RESIDUALS HIST(ZRESID) NORM(ZRESID).

DATASET ACTIVATE DataSet2.

DATASET CLOSE DataSet1.

EXAMINE VARIABLES=GlobalPSQI BY Urgency

/PLOT BOXPLOT STEMLEAF

/COMPARE GROUP

/STATISTICS EXTREME
/MISSING LISTWISE

/NOTOTAL.

=