SLEEP PROBLEMS IN PATIENTS ON PERITONEAL DIALYSIS

-PREVALENCE, EFFECTS ON DAILY LIFE AND EVALUATION OF NON-PHARMACOLOGICAL INTERVENTIONS

PIA YNGMAN-UHLIN

DEPARTMENT OF MEDICAL AND HEALTH SCIENCES

DIVISION OF NURSING SCIENCE

LINKÖPING

2011

Linköping University
FACULTY OF HEALTH SCIENCES

To Fredrik,
Rebecca & David

Supervisor	Ulla Edéll-Gustafsson, RN, Ass. Prof.
Co-Supervisor	Anders Fernström, MD. PhD.
	Sussanne Börjeson, RN, Ass. Prof.
Cover art	NASA photo gallery, a last quarter crescent moon above Earth's horizon 5 Sept. 2010. Expedition 24, International Space Station.
Illustrations	Pia Yngman-Uhlin
Typography	Claes Asker, PhD

Contact
Phone: + 46 101037792
Fax: + 46 13 123285
Email: pia.yngman.uhlin@liu.se

Address:
Pia Yngman-Uhlin
Division of Nursing Science,
Department of Medical and Health Sciences, Linköping University and
Department of Nephrology, County Council of Östergötland,
SE-581 85 Linköping
Sweden

ISBN 978-91-7393-207-3
ISSN 0345-0082
Dissertation 1233

Printed in Linköping, Sweden
by LiU-Tryck Linköping, 2011

-Some people can only dream about a good night´s sleep.

P Y-U

Preface

THIS THESIS IS BASED on work performed at the Department of Medical and Health sciences, Division of Nursing Science at Linköping University and Department of Nephrology, County Council of Östergötland.

With several years of experience working with chronic renal patients and mainly peritoneal dialysis treatment this thesis sprang up from the curiosity of how one can sleep sufficiently with a catheter in the abdominal cavity, sometimes connected to a machine. When I started to engage myself in the field I found that various uremic symptoms that trouble a person at dialysis treatment could interact with sleep and lead up to tiredness. The focus of this thesis became clear to me and I wanted to explore more about the sleep situation and the daily consequences of tiredness for patients treated with peritoneal dialysis at home. During the journey of research new questions arose and hopefully this thesis will contribute to further knowledge in this area.

Pia Yngman-Uhlin

Abstract

SLEEP PROBLEMS AFFECT a considerable number (49-86%) of patients undergoing peritoneal dialysis (PD) treatment. Insomnia i.e. difficulties to initiate and/or maintain sleep or too early wakening, combined with daytime symptoms, seems to be the dominating problem. Despite these facts there is a lack of research in PD-patients, especially studies with objective data on the sleep-wake cycle and evaluation of sleep promoting non-pharmacological interventions.

The overall aim of this thesis was to describe sleep problems from different perspectives, and how these problems affect daily life and health in patients treated with PD at home. The aim was also to evaluate an individualised non-pharmacological intervention for improvement of sleep quality outcomes.

Four studies were conducted during eight years, starting in 2002. Patients from six hospitals in the south-east of Sweden were invited to participate. In addition, data from a reference group with Coronary Artery Disease and a population group were used for comparisons with PD-patients in one of the studies. Data was collected by self-reported questionnaires, actigraphy registrations and interviews. Sleep was evaluated in a 17-week single-case study with an intervention focusing on sleep hygiene advice.

Data from a total of 700 sleep-wake cycles was collected in the patients' homes. The main findings clearly demonstrated that PD-patients have seriously fragmented sleep compared to the CAD- and population group, and that the PD-patients have a high prevalence of insomnia. The sleep was mainly disturbed by pruritus and Restless Legs Syndrome (RLS). Daytime impairments and a frequent napping behaviour were detected. The prevalence of fatigue was also reported to be extremely high. The patients described that an ever-present tiredness and poor sleep had

consequences in their everyday life both physically, mentally, socially and existentially. The nurse-led intervention demonstrated that individual, non-pharmacological sleep interventions can improve sleep and daytime activities in PD-patients.

This thesis elucidates that deteriorated sleep with serious fragmentation leads to a variety of daytime impairments and fatigue. By adopting “renal supportive care” in clinical work a more elaborate assessment and individualised non-pharmacological treatment of sleep problems may improve sleep quality and activity in frail patients undergoing peritoneal dialysis at home.

Keywords: fatigue, insomnia, peritoneal dialysis, renal supportive care, sleep, self-care management, sleep hygiene

List of Papers

THIS THESIS CONSISTS OF FOUR PAPERS, three have been published in international peer reviewed scientific journals, and one paper has been submitted. The papers will be referred to in the text by their roman numerals:

I. YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U: Self-reported subjective sleep quality and fatigue in patients with peritoneal dialysis at home. International Journal of Nursing Practice. 2006 Jun; 12(3):143-52.

II. YNGMAN-UHLIN P, FRIEDRICHSEN M, GUSTAVSSON M, FERNSTRÖM A, EDÉLL-GUSTAFSSON U. Circling Around in Tiredness: Perspectives of Patients on Peritoneal Dialysis. Journal of Nephrology Nursing. 2010 Jul-Aug; 37(4):407-13.

III. YNGMAN-UHLIN P, JOHANSSON A, FERNSTRÖM A, BÖRJESON S, EDÉLL-GUSTAFSSON U. Fragmented sleep – An unrevealed problem in peritoneal dialysis patients. Scandinavian J Urology and Nephrology. 2011; 45, 206-215

IV. YNGMAN-UHLIN P, FERNSTRÖM A, BÖRJESON S, EDÉLL-GUSTAFSSON U. Evaluation of an individual sleep intervention program in peritoneal dialysis patients (submitted).

ADDITION:

BESIDE THE PUBLICATIONS IN THIS THESIS, part of the material and additional findings have been presented or published.

YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U. Self-reported sleep, daytime functioning and tiredness in peritoneal dialysis therapy at home. *Region meeting in nephrology*, Linköping 1-2 April 2004.

YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U, Self-reported sleep quality, fatigue and daytime symptoms in patients undergoing peritoneal dialysis at home. *17th Cong of European Sleep Research Soc.* Prague, Czech Republic 2004 Oct 5-9.

YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U, Self-reported sleep quality, fatigue and daytime symptoms in peritoneal dialysis therapy. *Swedish nephrology nursing association (SNSF) Spring meeting* in Linköping, 29-31 May 2005.

YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U. Self-reported sleep and fatigue in patients suffering from uraemia. SSF (network for sleep and Health) Linköping: 25 Oct. 2005.

YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U. Self-reported sleep quality, fatigue and daytime symptoms. *A celebration event, Med dr h c professor Afaf Meleis and Twenty Years of Nursing Science*. 29-30 Nov. 2007, Linköping.

YNGMAN-UHLIN P, FERNSTRÖM A, EDÉLL-GUSTAFSSON U. Are PD-patients Sleepy, depressed or suffering from fatigue? *European Renal Association-European Dialysis and Transplant Association, ERA-EDTA XLV Congress*, 10-13 May 2008, Stockholm, Sweden.

YNGMAN-UHLIN P. (Invited speaker) Sleep in peritoneal dialysis patients, PD-in practice, National network meeting, Enköping, Haga castle 1-2 Sept. 2008.

YNGMAN-UHLIN P, FERNSTRÖM A, EDÉLL-GUSTAFSSON U Are patient in peritoneal dialysis treatment just sleepy? *19th Congress of European Sleep Research Society*, Glasgow, 2008 Sept. 9-13.

YNGMAN-UHLIN P. (Invited speaker) Experiences of tiredness in peritoneal dialysis treatment. *SSF (network for sleep and Health)* Linköping: 21 Oct. 2009.

YNGMAN-UHLIN P, EDÉLL-GUSTAFSSON U, BÖRJESON S, FERNSTRÖM A, UHLIN F. Fatigue and depression in PD and HD patients. *American Society of Nephrology ASN, Renal week.* Nov 2009, San Diego, USA

YNGMAN-UHLIN P. (invited author) Sleepiness and tiredness a serious problem for PD-patients. *Incitament* 2010 (19);1:57-59. (In Swedish)

YNGMAN-UHLIN P. (invited speaker) Sleep problems in PD-patients. Winter meeting for PD-nurses. Hotel Baltic, Sundsvall 16-17 Mars 2010.

YNGMAN-UHLIN P. (invited speaker) Tired but can´t sleep. Renal medicine Spring conference, Kalmar 2-4 May 2010.

Contents

Abbreviations

APD – Automatic Peritoneal Dialysis
CAD – Coronary Artery Disease
CAPD – Continuous Ambulatory Peritoneal Dialysis
CCPD – Continuous Cyclic Peritoneal Dialysis
CKD – Chronic Kidney Disease
EEG – Electro Encephalon Graphy
ESRD – End Stage Renal Disease
HD – Haemodialysis
HRQoL – Health Related Quality of Life
MET – Metabolic Equivalent Unit (Kcal/kg/hour)
MFI – Movement and Fragmentation Index
PD – Peritoneal Dialysis
REM – Rapid Eye Movement
RLS – Restless legs Syndrome
SE – Sleep Efficiency
SWS – Slow Wave Sleep
USI – Uppsala Sleep Inventory

Introduction

THIS THESIS FOCUSES ON PATIENTS UNDERGOING peritoneal dialysis (PD) treatment at home. This condition is more or less linked with a multitude of problems associated to their End Stage Renal Disease (ESRD) and life supporting treatment where practically every aspects of life is affected. Physically there are still functions of the native kidney that cannot be replaced, which results in symptoms of uremia more or less still remaining. Psychologically, problems encountered by the patients and their families means having to deal with an uncertain future, worries about the high risk of complications and a premature death.

Sleep problems can be seen as a general problem that can affect all people in different situations through their life. Sleep is a physiological state that cannot be brought on by will and is necessary for survival since many rebuilding processes take place during that time. Knowledge about sleep is advancing in many populations including ESRD and haemodialysis (HD) populations but are more lacking in PD-populations. Many patients on peritoneal dialysis treatment are physically deconditioned from the chronicity of their disease and by co-morbidities. In addition their situations can be complex with a high burden of general uremic symptoms and symptoms related to disturbed sleep such as daytime sleepiness, tiredness or fatigue. Notwithstanding a sometimes poor condition the patients are responsible for an extended self-care management at home.

This thesis may contribute to the body of knowledge in both sleep research and peritoneal dialysis patients.

Background

FOR PATIENTS WITH ESRD both the treatment and the illness can be challenging. The final stage of chronic renal failure is fatal if left untreated because the kidneys are no longer able to remove waste products and water in a sufficient proportion from the body. To survive, two therapy options are available; dialysis or transplantation.

Transplantation can be done by an organ from a living or deceased donor and dialysis can be managed in two modalities, haemodialysis or peritoneal dialysis. For the patients this means being treated but not cured and the illness is put demands on both the patient and the family.

In December 2009 the number of patients treated for ESRD in Sweden was 8205. Of these 4606 were living with a transplanted kidney and 3599 underwent dialysis treatment, 2760 on hemodialysis and 839 on peritoneal dialysis[1].

Peritoneal dialysis treatment

The first clinical application of peritoneal dialysis was conducted by Georg Ganter in 1923[2]. In 1959 Paul Dooland developed a polyethylene catheter for peritoneal dialysis treatment to be used in the Korean battlefield war[3]. The first reported successful peritoneal dialysis treatment using an indwelling catheter in a human was later reported when Richard Ruben took advantage of the Dooland technique. A female patient was first to repeatedly be dialysed at home with successful improvement[4]. Development of a nylon catheter with perforations at the curved end was the start of a commercially available product in 1964[5]. The evolution of Continuous Ambulatory Peritoneal Dialysis (CAPD) started in 1976 when Robert Popovich and Jack Moncrief worked out the kinetics of long-dwell equilibrated dialysis[6]. Later on in the early 1980s automated PD in form of

continuous cyclic peritoneal dialysis (CCPD) was developed by Diaz-Buxo[7].

Today the technique has been established and has grown. However, in 1976 approximately only 800 patients were undergoing PD-treatment worldwide[8] which is only an approximate about the same as the total number of PD-patients in Sweden 2009[1]. At the end of 2008, the prevalence of PD treatment varied between eight (Montenegro) and 115 (Denmark) per million population. Sweden was placed second from the top with 91 per million population[9]. The choice of treatment varies between countries partly due to the reinvestment and healthcare systems.

The commonly used regime today is the one entailed by Moncrief, where about two litres of dialysis solution is drained and refilled into the peritoneal cavity during four exchanges over a 24-hour period (Figure 1). This procedure requires patient self-care management skills.

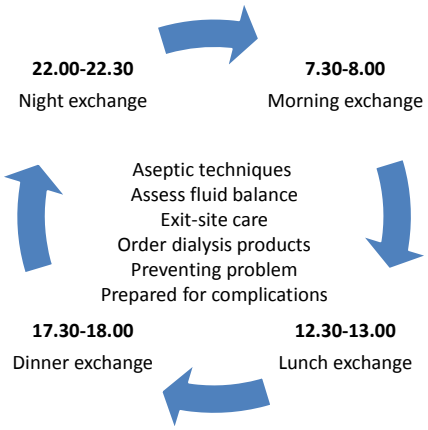

Figure 1. PD-patients responsibilities in the treatment and the manual PD-cycle with four exchanges during different time periods of the day.

Manage the treatment

The physiology of peritoneal dialysis is relatively simple. The peritoneal membrane has a surface area of up to 2 m^2 and covers the peritoneal cavity. By a surgically inserted catheter two litres of dialysis fluid is instilled and left for dwelling. After the dwell time the dialysate is drained and fresh

dialysate is instilled again, a procedure that takes place four times a day. For the patients the exchange procedure takes about 20-30 minutes to complete and the patients customise the treatment to suit the daily life activities. Uremic toxins and solutes are removed by diffusion from the bloodstream in the peritoneal membrane. Fluid (water) is removed by osmosis and the amount of fluid removed mainly depends on the concentration of the osmotic gradient (glucose) where three concentrations are available[4]. The patients choose a higher concentration of the solution if a higher amount of body-water must be removed.

The other option is that a machine automatically controls the fill volume, dwell time and length of treatment during the night. Both modalities claim to have a solid control of the fluid balance and aseptic management. The patient also needs to prepare for and prevent complications. Most importantly, an aseptic technique is required for the exchange as a critical moment occurs when the transfer-set is open in order to avoid infections i.e. peritonitis.

The modern PD-regime is flexible and allows combinations of daytime exchange and night machine as well as a session of supporting haemodialysis in between.

Being a peritoneal dialysis dependent person

Being a dialysis dependent person means that health is sustained but not restored. The chronic renal disease is a progressive loss in renal function over a period of months or years. Dialysis treatment mostly demands restrictions on food and liquid intake, food restrictions and multi-pharmacy. Psychological stressors have been identified in a Swedish dialysis population such as lack of freedom, lack of control, loss, and brooding[10].

The uremic intoxication, caused by decreased renal function, involves the body homeostasis, all organ and organ systems which produces a multitude of symptoms (Figure 2)[11]. Despite the dialysis treatment the uremic symptoms is remain more or less. Consequently, the symptom burden in uraemia is a serious issue with substantial impairment in

physical and mental health[12]. A trend towards a greater overall symptom burden for women in haemodialysis has been shown where a median number of symptoms were 10.5 compared to men 8.0[12].

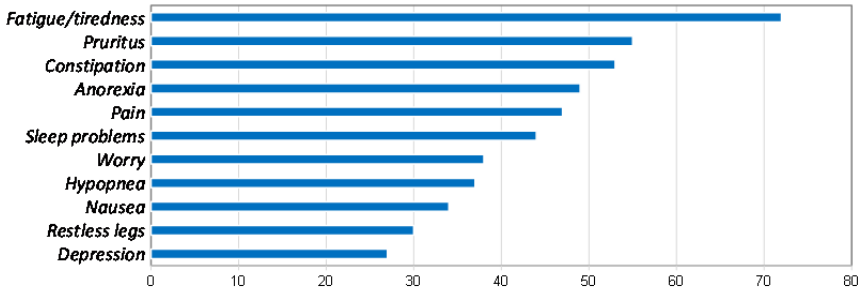

Figure 2. Weighted mean prevalence (%) of symptoms among dialysis patients. Data from a systematic review of 59 studies[11](page 85). Reproduced with permission from the publisher.

Multiple symptoms can occur together and be experienced simultaneously. The experience of the effects from the symptom can be multiplicative rather than additive which is explained in the theory of unpleasant symptoms by Lenz and co-workers[13]. Factors contributing to the symptoms can be categorized as physiological, psychological and socio-demographic. Those factors affect four dimensions that are common across symptoms and are experienced by the patient; intensity, duration, distress and quality[13]. Intensity or severity is most often assessed clinically with different rating scales. Duration refers to the persistence or the frequence of the symptoms. Distress refers to how bothered patients are by the symptoms. It is this dimension that affects quality of life the most[13]. Finally, the quality of the symptom is often reflected by the adjective used by the patients in the symptom description or the location of the symptom[13].

Self-care management

For a PD-patient healthcare providers are important in the pre-dialysis, educational, training and self-management phases[4]. It is important that the patients leave the medical ward with knowledge to care safely for themselves. According to Riegel (2009) self-care refers to the behavioural to maintain health (self-care maintenance) and the decision behaviour to manage occurring symptoms (self-care management)[14]. A complex series of behaviours take place in the self-care management and several abilities are required in the decision process about self-care management which can be altered by decreased sleep quality. To gain knowledge and comprehension about symptoms, cognitive and mental processes are important functions. Those functions incorporate thinking, knowing, remembering, judging, and problem solving[14]. PD-patients have described two domains in self-management as being important; having autonomy and control of their healthcare and to achieve a normal everyday life[15]. Patients further have reported that self-management has both positive and negative effects[16]. Positive effects were; the freedom to carry on with daily activities and the convenience of a simple treatment at home. The negative aspects were being tied up by a time-consuming treatment, risks for complications, burden of responsibility and home modifications due to the treatment, changes in body image and physical restrictions[16]. A supportive and educational system that could be used for assistance in decision making and behavioural control should be available in the care for the patients.

Renal supportive care

Supportive care is a concept closely associated with cancer patients and palliative care. Studies about renal supportive care also refer to end of life treatment[17, 18]. However, in a concept analysis by Noble and co-workers[19] it is concluded that renal supportive care is a dynamic and emerging concept that can be used for complex goals to be realised by multidisciplinary teams together with the renal patients and could be integrated in everyday practice[19]. This is the basis for this thesis. One illustrative example of renal supportive care has been reported from Hong

Kong where a nurse-led case management programme based on motivational interviews before and after discharge and with regular and supporting phone calls was evaluated. The report showed statistically significant improved HRQoL domains, social function and sleep compared to a control group[20]. It has further been suggested that an effective communication and a working partnership with the PD-patients is crucial to achieve a better treatment outcome and to meet each patients individual needs[21].

The Swedish Kidney Association (RNj) has worked out guidelines for the care of kidney patients[22]. They claim that the care must be provided in such a way to encourage patients to take responsibility for their treatment as far as possible and their next of kin must be given the opportunity to participate in the treatment. Furthermore the patients are entitled to a multi-disciplinary team, an individual care plan, an responsible physician and 24-hour access to nephrology staff[22]. This emphasises the importance of individuality in the treatment and that the safety for their patients, and the next of kin, is prioritised. At the time of the introduction of the PD-treatment RNj further recommend a house-call to every patient[22] which further facilitate an individualised treatment. Patients´ extended and required self-care management abilities are dependent on a supportive renal care. These were the assumptions in the performance of the intervention study (page 45).

Normal Sleep

Sleep is a universal phenomenon involving all human beings. According to a behavioural definition sleep is a reversible behavioural state of perceptual disengagement from an unresponsiveness to the environment[23], or a temporary loss of consciousness[24]. According to a physiological definition sleep is characterised by dynamic fluctuations in the nervous system as well as in the haemodynamic respiratory and metabolic systems[24].

Sleep stages and circadian rhythms

The architecture of normal sleep consists of five different sleep stages; rapid eye movement- (REM) sleep and non-REM sleep. The non-REM sleep consists of 4 stages (Figure 3).

The changes in sleep stages is a gradual process and the change through the five stages is termed a sleep cycle. One sleep cycle has a duration of 70-90 minutes and the normal number is five sleep cycles per night[23].

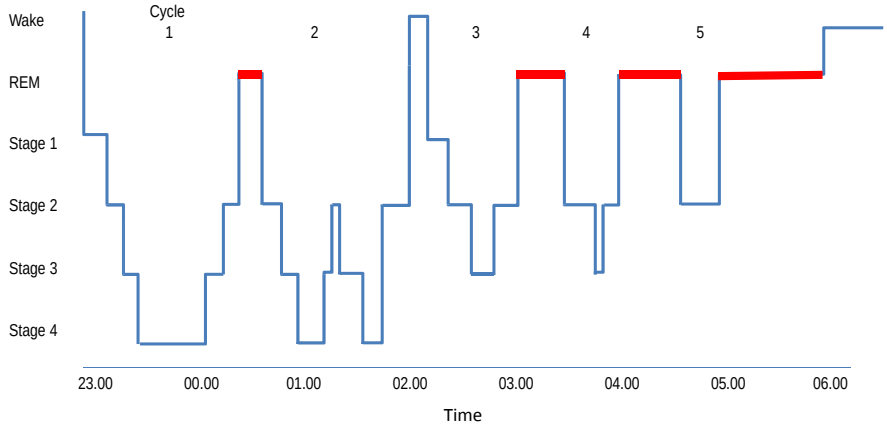

Figure 3. A hypnogram, showing distribution of deep sleep (stage 3 and 4), light sleep (stage 1 and 2) and Rapid Eye Movement (REM=bold line) sleep i.e. dream sleep during a 7-hour sleep period.

Stage 1 is drowsiness and is a transition stage into sleep. Stage 2 is light sleep. Stages 3 and 4 are the deep sleep also known as the slow-wave-sleep (SWS) referring to the slow curves indicated by the Electroencephalogram (EEG). During REM sleep there is a loss of core muscle tone and the brain activity is comparable to wakefulness[23].

The need for sleep varies between individuals, but the amount of sleep required for adults is about six to eight hours[25]. A decreased amount of sleep and impaired sleep quality results in daytime sleepiness[26]. During a person´s lifespan the sleep architecture is reformed which means that elderly individuals have less SWS and more awakenings i.e. more fragmented sleep than younger individuals[27, 28]. Sleep deprivation, which is

a loss of deep sleep, alters the sleep quality negatively but sleep deprivation is normally recovered by a physiological re-bound effect[29]. This function re-distributes the amount of sleep time to longer periods of deep sleep (stage 3 and 4) and REM-sleep while sleep in stage 2 is shortened and stage 1 may disappear completely [29]. The amount of sleep is reported to be decreasing in adults. In a review study Knutson and Van Cauter found that during a period of 35 years the sleep duration dropped from 8.9 hours in mean of sleep time (1960) to 7 hours (1995)[30] in a US population.

Circadian rhythms are a fluctuation of several bodily functions that recur in a cycle of about 24 hours. The sleep-wake cycle is the variation between sleep and wakefulness and follows the circadian rhythm. This rhythm is regulated by internal, endogenous systems and is synchronised by the master circadian pacemaker i.e. the suprachiasmatic nucleus situated in the anterior hypothalamus in the brain[24]. The circadian clock also needs to be synchronised to the environment. This is done to the daylight[24]. The hormone melatonin is secreted during the night and inhibited by light during the day. This system is called the external clock[31]. The circadian sleep-wake cycle has been described as periods of high and low sleep propensity that is the urge to fall asleep[32, 33]. This also include a period of higher sleep propensity in the afternoon named *nap zone*[33]. Sleep follows the circadian rhythm of body temperature and is initiated when the body temperature is falling and the wake-up appears when the temperature is rising[32-34].

Disturbed sleep in peritoneal dialysis

In peritoneal dialysis patients sleep problems is a prevalent problem and has been reported in 49-86% of the patients[35, 36]. Compared to HD-patients, with a sleep problem prevalence of 49-88%[37, 38], there is only a small difference between the two dialysis modalities.

Insomnia seems to be the most prevalent of the sleep problems in dialysis patients (69%) followed by obstructive sleep apnoea syndrome (OSAS) (24%)[39, 40]. Persistent insomnia problems consist of difficulties to

initiate the sleep (early insomnia), maintain sleep (middle insomnia) or waking up too early in the morning (late insomnia) resulting in daytime sleepiness.

The prevalence of insomnia is high in both PD- and HD-patients compared to a general Swedish population where insomnia was recently reported in 6.8%[41] and a Spanish population where insomnia was reported in 6.4%[42].

Despite the high prevalence of insomnia in PD-patients there is a lack of research that objectively evaluates the sleep-wake cycle in this group. Only one study has been found that objectively evaluated the sleep-wake cycle for seven consecutive days by actigraphy (actigraphy is described on page 37) in a small PD-sample (n=6)[31]. This study showed decreased sleep efficiency and increased nocturnal wake time. This scarce research in PD-patients warrants further studies in larger populations.

Insomnia is a prevalent problem in dialysis patients. However, no consensus has been reached regarding the definition of insomnia. Three diagnostic systems are used; Diagnostic and statistical manual of mental Disorders (DSM)-IV[43], International Statistical Classification of Diseases (ICD) -10[44] and International classification of Sleep Disorders[45]. The definition by the Swedish Welfare State is; sleep onset latency >30 minutes, sleep duration <6 hours, five or more nocturnal awakenings or nocturnal awakenings >45 minutes combined with more than one daytime symptom[46]. This definition corresponds to the ICD-10 classification and is adopted as the definition of insomnia in this thesis.

The high prevalence of sleep problems in dialysis patients has partly been addressed to restless legs syndrome (RLS) which is a well-known sleep disturbing factor and also prevalent in dialysis patients[47].

RLS is a movement disorders which can be primary or secondary[48]. Primary RLS or idiopathic RLS occurs without any background condition whilst secondary RLS affects pregnant women, patients with end stage renal disease, iron-deficiency anemia, and children with attention deficit hyperactivity disorder[48]. RLS diagnosis is based on four clinical criteria: 1) An urge to move the legs that is impossible to resist 2) The RLS symptom starts or become worsened when resting 3) the symptoms are relieved by

moving 4) and the symptom is worse in the evening or during the night[49]. RLS has further been suggested to mean “restless-limb syndrome” since the restless symptoms can also affect the arms[50]. In dialysis patients, RLS has been shown to cause significantly reduced Quality of Life (QoL) and in a Kaplan-Meier analysis dialysis patients with severe RLS had 39% greater hazard of death[47].

Another common complaint in dialysis populations is pruritus. This distressing symptom has a higher prevalence in patients on dialysis treatment than pre-dialytic patients[51]. Data from a large study in 7 countries with more than 6000 HD patients showed a prevalence of moderate to extreme pruritus in 46% of the participants[52]. Sixty percent of the patients reported that they were aggravated by pruritus during the night and 46% had daily itching bouts[53]. No significant differences were found between HD- and PD-patients[54] which makes pruritus a symptom of disturbed sleep for all dialysis patients. Patients bothered by pruritus spend significantly more time awake during the night compared to those without pruritus, $p<0.002$[52]. Wikström (2007) further emphasised that the relationship between pruritus and mortality was decreased when an adjustment for sleep was done and also suggested that poor sleep is a pre-dominating characteristic between mortality and pruritus[52]. More research on the impact of RLS and pruritus on sleep in PD-patients are warranted, especially by objective assessments.

The most general treatment for insomnia is hypnotics[55, 56] which has side-effects such as daytime sleepiness, dependency and drug-drug interactions[57]. Only 23% of haemodialysis patients with sleep problems had medication documented for that symptom[58] which probably indicates serious under-treatment. However, there are non-pharmacological treatment options, such as cognitive behavioural therapy (CBT), which has become more established and is suggested to be a standard treatment either alone or in combination with hypnotics[59]. In elderly individuals sleep behavioural therapy has been more effective than hypnotics[60]. Applying CBT treatment in PD-patients might be a good option since the renal failure alters drug absorption, drug metabolism and often results polypharmacy. In HD-patients sleep quality was improved by increased

physical activity alone[61]. There is lacking knowledge about treatment interventions in PD-patients with sleep problems and only one pilot-study has been found using CBT and hypnotics in PD-patients and showed positive effects on insomnia. This study only used subjective assessments[62] so consequently research with objective assessments is required in PD-patients.

Sleep deprivation and impaired sleep quality

The purpose of sleep has not fully been elucidated. Theories have suggested physical restoration, energy conservation and regulation of immune functions as well as resolution of emotional stress and consolidation of memory[63]. However, the importance of sleep for mental and physiological processes has been demonstrated in several studies. Sleep deprivation has several negative consequences. In a clinical review study daytime symptoms such as fatigue, negative mood, decreased attention and abilities to concentrate were related to insomnia[64]. During prolonged wakefulness i.e. total sleep deprivation, cognitive functions such as attention[65] and being easily distracted[66] result in decreased performance and impaired cognitive processing[67]. These are important functions for patients with extended self-care management responsibilities since individuals with decreased sleep quality need more time to perform tasks and they further make more mistakes[25]. Furthermore, fragmented sleep produces negative mood changes[68]. Physiologically deep sleep is certainly important. Sleep fragmentation caused by sleep apnoea has been reported to alter a variety of harmful processes in chronic kidney disease. For instance, hypoxemia due to apnoea activates the sympathetic nervous system and the renin-angiotensin-aldosterone system which alters cardiovascular damages by increased blood pressure[69]. There might be underestimations of sleep problems in dialysis patients due to the complex symptom burden with overlapping and coexisting symptoms.

Furthermore, an association between immunological processes and sleep has been suggested[70]. In HD-patients it is reported that C-reactive protein is significantly higher in patient-reported bad sleepers than in good

sleepers[70]. Since the cause of mortality in dialysis patients is dominated by cardiovascular diseases (36%) and infections (15%)[1] those consequences of sleep problems may also be considered.

Fatigue and tiredness

In addition to impaired sleep quality daytime symptoms are often reported and expressed as tiredness, sleepiness or fatigue. Fatigue may be related to the primary disease process or a secondary phenomenon. No universal definition for fatigue exists and fatigue therefore has various definitions with similarities in health-related disciplines. Tack [71] has defined fatigue in rheumatoid arthritis patients as a subjective sensation of generalised tiredness or exhaustion. Piper[72] defined fatigue as a perception of a complex interplaying of both somatic and psychological factors. Both definitions offer a holistic concept. Tack[71] further emphasises the subjective nature of the symptom. Another study has adopted fatigue as a central or peripheral phenomenon[73] and Jhamb and co-workers (2008) presents fatigue as a continuum with energy and vitality at one end and fatigue and exhaustion at the other end[74].

Similar concepts such as tiredness and weakness are often used as synonyms for fatigue but the definitions of tiredness are even more lacking. Ream and Richardson's concept analysis of fatigue conclude that tiredness can provide an indication of fatigue but is not synonymous, tiredness is more of a normal and temporary lessening of strength and energy which is an indication for rest[75]. Sleepiness is defined as a state of physiological need for sleep, and its intensity is evidenced by how rapidly sleep onset occurs, how easily sleep is disrupted, and how long sleep endures. This need for sleep can cause involuntary sleep during the day in situations with low activity[23]. According to those definitions, fatigue cannot be relieved by sleep and does not have the protecting function as does tiredness[76]. Fatigue has further been suggested to have a connection to chronic illness[77]. In ESRD fatigue can partly be related to the high prevalence of sleep problems but other contributing factors have been suggested; physiological, behavioural, treatment-related and individual characteristics [74]. There is a lack of knowledge about associations between

fatigue and sleep problems in PD-patients but there are studies conducted with mixed PD- and HD-populations. In HD-patients low levels of physical activity and frequent symptoms were related to increased fatigue score[78]. The prevalence of fatigue in ESRD patients has been reported to be seriously high and had a weighted mean prevalence of 71%, range 12-97, in eleven studies conducted with PD-patients and HD-patients[11]. It should be noted that the studies have either measured tiredness or fatigue. This demonstrates the problem with inconsequent definitions. In this thesis the definition of fatigue by Cella and co-workers is adopted:

> "*…diminished energy and mental capacity and increased need to rest that is disproportionate to any recent change in activity level and is evident nearly every day during any 2-week period in the past month."*[79] *page 528*.

Regarding tiredness, the description of the phenomenon by Hetta and co-workers was adopted in this thesis; physical tiredness, mental tiredness and exhaustion[80].

Health related quality of life

Disease, symptoms and treatments have an impact on everyday life. The concept "Health related quality of life" (HRQoL) has been well established in research during the last decade. When searching for the term in the title or abstract on PubMed, the number of hits has increased more than fivefold from 1990-1999 (2321) compared to 2000-2010 (17849). This indicates that the aspect of the overall impact of diseases on health has been accepted as an important outcome. However, an increased use of HRQoL questionnaires in research has not been adopted in clinical practice to the same extent.

Sleep problems negatively affect HRQoL in general populations[81, 82] as well as in renal transplanted patients[83, 84]. In a PD-population sleep quality was negatively correlated to quality of life (QoL)[84]. Factors contributing to HRQoL in ESRD has been described; *demographic factors*; *behavioural factors* such as; use of nicotine, physical and leisure activity, substance abuse, and social support, *symptom burden*; including sleep disturbances

and fatigue and *frailty*; including co-morbidity and other physiological alterations[85]. The common conceptualization of HRQoL has been based on the World Health Organization's definition of QoL as "…*a complete state of physical, mental, and social well-being and not merely an absence of disease in infirmity"* [86] page 7. This definition was adopted by 61 states at the International Health Conference in 1946 and has not been modified since 1948[87].

Based on the definition by the WHO Unruh and Hess presented a HRQoL model in the treatment for CKD, including the three dimensions stipulated by the WHO[88]. The physical dimension includes physical activity, fatigue/sleep, symptoms and appetite. The psychological dimension refers to stress, anxiety, distress and cognitive functions and the social dimension refers to family relationships, vocational role and sexual role[88]. In addition, Unruh and Hess[88] (2007) constructed a surrounding area of global quality of life including domains related to perceived health, daily functioning, happiness, satisfaction and spirituality which might not be affected by the health[88].

PD-patients are a group of frail patients who take responsibility for their treatment at home and are burdened with symptoms affecting all dimensions of life. One key point is the decreased sleep quality which is affected by other symptoms and *per se* affects the experience of those. This is challenging for the healthcare providers to improve, through strengthening patients´ self-care management behaviour and by providing supportive care.

Aims of the thesis

THE PURPOSE OF THIS THESIS WAS TO DESCRIBE sleep problems from different perspectives, and how these problems affect daily life and health in patients treated with peritoneal dialysis at home. The objective was also to evaluate a non-pharmacological intervention for improvement of sleep quality outcomes.

The specific AIMS of the studies were to:

I describe habitual sleep, daytime symptoms, sleep disturbing factors, current sleep during one week and fatigue in patients with peritoneal dialysis treatment at home and also to discover predictors for sleep quality outcome.

II describe how patients in peritoneal dialysis at home experience how tiredness and sleepiness affect their daily life.

III describe the sleep-wake cycle, sleep quality, fatigue and health related quality of life in patients with peritoneal dialysis treatment at home. Further, to explore differences compared to patients with coronary artery disease and individuals from the general population.

IV evaluate effects of individually designed non-pharmacological interventions on sleep, activity and symptoms of fatigue in peritoneal dialysis by use of both actigraphy and patient-assessed questionnaires.

Methods

THE PATIENTS IN STUDY **I-IV** WERE SELECTED from six hospitals in the south-east of Sweden, two university hospitals, one county hospital and tree districts hospitals.

Subjects

Inclusion criteria for the PD-patients were: duration of PD treatment at home for two months or longer (**IV**) or three months or longer (**I-III**), being over 18 years of age, ability to read and understand the Swedish language, no known abuse of alcohol and/or drugs (**I-IV**), no malignancy, no persistent sequelas from stroke or any other disorder of importance and no current treatment for mental disorder (**III-IV**). In study **II** a purposeful sample was used, which is in accordance with phenomenology[89] to obtain a sample variation regarding age, gender and number of month on PD treatment.

In study **III** a reference group consisting of 22 patients suffering from chronic Coronary Artery Disease (CAD) was included. They were derived from a larger study (n=680) with a history of stable angina pectoris (Canadian Cardiovascular Society Class I-II), listed for percutaneous coronary intervention at a University Hospital in the south east of Sweden. As uraemia is a chronic disease like CAD, which also is prevalent in uraemic populations, a comparison with a group of CAD patients was included. Data from those patients were collected two years after a CAD intervention. Inclusion criteria were identical to the PD-patients in study **III** except for the PD-treatment. A matching by age, gender and month for data collection was performed since the daylight in northern Europe varies substantially during the year. In addition, 18 individuals from a general

population group recruited from the Swedish Government Person and Address Register Database. They were matched controls to the CAD group in a previous study[90] consequently also matched the PD-patients. Number of patients (PD) and characteristics in study **I-IV** are presented in table 1. One PD-patient participated in both study **I** and **II**. For study **I-IV** all data were collected within a time period of 8 years (2002-2010).

*Table 1. Patient characteristics for the PD-patients in study **I-IV**.*

	Study I n=55	**Study II** n=14	**Study III** n=28[b]	**Study IV** n=9
Age (mean, SD)	63 (14)	58.9 (13.3)	61.7 (8.7)	65.4 (12.4)
Gender (n) (Male/Female)	41/14	6/8	16/12	7/2
Treatment modality (APD / CAPD) (n)	16/39	5/9	9/21	3/8[a]
Working (n)	12	2	9	2
Sick leave (n)	12	2	2	1
Retired (n)	31	5	17	6
Married/cohabit (n)	42	11	24	7
Diagnosis[c] (n)				
Glomerulonephritis	15	6	9	1
Polycystic kidney disease	10	-	2	2
Nephrosclerosis	10	2	1	2
Diabetic nephropathy	8	3	11	2
Chronic pyelonephritis	2	-	1	-
Others	14	3	10	2
Regular use of hypnotics (n)	10	No data	13	2
Regular use of nicotine (n)	21	No data	10	1
Duration of treatment (month, SD)	23.8 (17.6)	25.2 (19.2)	19 (18.5)	24.6 (26.3)

*[a]=Two patients had a combination of Continuous Ambulatory Peritoneal Dialysis (CAPD) and Automatic Peritoneal Dialysis (APD) and one patient had a combination of APD and one weekly session of Haemodialysis (HD).[b]=number of PD-patients include. In addition two matched reference groups also participated in study **III** 22 Coronary Artery Disease (CAD) patients and 18 individuals from the general population.[c]=Some patients had more than one renal diagnosis.*

Designs

In this thesis four studies were conducted. Study **I** and **III** were descriptive, cross-sectional multicentre studies where the study variables were captured once during one period of data collection. In study **III** a correlational and comparative design was utilised with two reference groups. In study **II** a qualitative descriptive phenomenological design was applied. The fourth study (**IV**) was a single-case study with an AABBC non-randomised experimental design. The A phases were two multiple

baseline data collections, the B phases were intervention phases and the C phase was a non-treatment phase with a follow-up.

Measurements

A total of 55 (**I**), 470 (**III**), and 515 (**IV**) sleep-wake cycles were assessed using both objective (**III, IV**) and subjective data collection (**I-IV**).

Actigraphy

Actigraphy is a non-invasive technique that allows assessment of estimated sleep-wake parameters for extended periods and is therefore useful for studies in the home environment. It is a simple device for the patients to apply at the wrist or the upper arm. To distinguish sleep from wakefulness by body movement the assumption is that activity i.e. body movement indicates wakefulness and conversely a motionless period precedes sleep.

Two types of actigraphs were used, first, Actiwatch-L® (Cambridge Neurotechnology Ltd) (**III**) and later on a more developed device, SenseWear pro® (Bodymedia, Pittsburgh, PA) (**IV**) (Figure 4a and 4b). Both are computerised accelerometers and measures limb movements.

*Figure 4a. Actiwatch-L® applied at the wrist (**III**).*

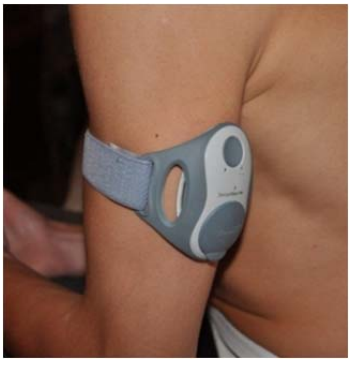

*Figure 4b. SenseWear pro® applied at the upper arm (**IV**).*

In study **III** all participants wore Actiwatch-L® at the wrist for seven days at the non-dominant arm. Every second 32 samples of the amplitude are

checked and the highest amplitude is saved as the peak intensity. By use of advanced algorithms a high sensitivity for other parameters can be generated (Table 2). Data were processed in the software package *Actiwatch Sleep Analysis 2001*, version 1.9[91].

*Table 2. Description of actigraphy variables measured by the two actigraphs used in study **III** and **IV**.*

Variables	*Description*	*Scale and cut off*
Sleep variables [a,b]	Bedtime, sleep latency, wake time during night, number of wake bouts, sleep duration and nap time.	-
Movment and Fragmentation index (MFI) [a,b]	This index is an indicator for disrupted sleep i.e. percentage of minutes moving + percentage of immobility.	>50 = poor sleep, <20 = good sleep.
Sleep efficiency (SE) [a,b]	Ratio of actual sleep time divided by time in bed expressed in per cent.	<85% = poor sleep
Interdaily stability [a]	Quantifies the degree of similarity concerning the activity between individual days.	Range; 0-1. Values of 0,6 = normal.
Interdaily variability [a]	Quantifies the fragmentation of periods of rest/sleep and activity/wakefulness. A higher value is similar to more fragmented rhythm.	Range; 0-2, <1= typical value
Amplitude of the rhythm (AMP) [a]	Differences between the average activity of the five least (night) and the ten most (day) active hours, are sensitive to the overall activity.	-
Relative amplitude [a]	Ratio of AMP and average activity of the five least and the ten most active hours gives a correction for the sensitivity.	Range 0-1, values close to 1= more active rhythm.
Activity [b]	Number of steps, minutes of moving, minutes of immobility	-
Energy expenditure [b]	Metabolic Equivalent Unit (METs) Kcal/Kg/hour	Watching TV=1.1 Walking =4.1, Running=9.5

[a]=Actiwatch-L®, [b]=SenseWear pro®

SenseWear pro® actigraph was designed to be worn at the upper arm under clothing and was used in study **IV**. Physiological body signals were registered by four sensors every minute; skin temperature, galvanic skin response, heat flux and a 2-axis accelerometer. Information from the

sensors was processed in the software program SenseWear® 6.1 (Bodymedia Inc.) where algorithms calculated sleep and activity variables (Table 2).

For each night a movement index (MI) and fragmentation index (FI) were calculated. In addition movement and fragmentation index (MFI) were calculated where an index more than 50 indicates serious fragmentation and below 20 is a well consolidated sleep[92].

$$MFI = \left[MI = \frac{Minutes\ of\ moving}{Time\ in\ bed} x100\right] + \left[FI = \frac{One\ minute\ of\ immobility}{Total\ number\ of\ immobility\ phases} x100\right]$$

In addition visual graphs of the sleep wake-cycles were delivered from the program (Figure 5). These were used to motivate and educate the patients (**IV**).

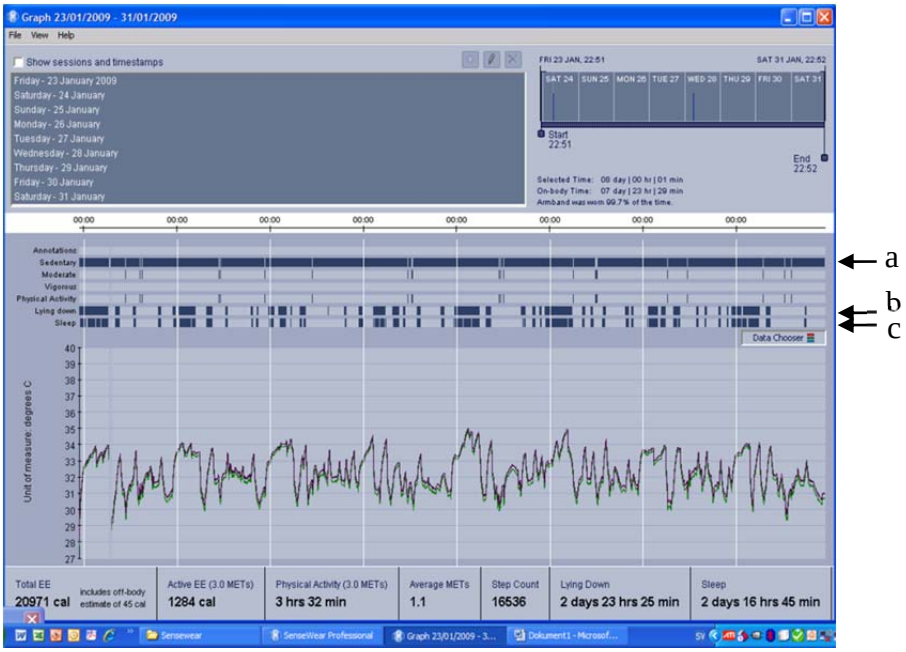

*Figure 5. A screen illustration from a single one-week, SenseWear®-registration. Arrow points out level of activity (a), lying down position (b) and sleep pattern (c) where the dark field indicates activity, lying down position and sleep. This screen was used to visualise the sleep problem and motivate the patients in the intervention study (**IV**).*

Questionnaires

Self-reported data were collected by four validated questionnaires and one study specific sleep diary (**I, III, IV**). Additional information about diagnosis and biochemical parameters was collected from the patients´ records at the time for data collection (**I-IV**). Data regarding validity and reliability for the questionnaires is presented on page 50.

Uppsala Sleep Inventory

To assess the habitual sleep during the last four weeks, Uppsala Sleep Inventory (USI)[80] was used in a modified version (**I, III, IV**). The questionnaire measures sleep variables; bedtime, sleep onset latency (time from light off to falling asleep), nocturnal awakenings (n), morning awakening (time), sleep duration (h), assumed sleep duration (h), numbers (n) and duration (h) of naps, if the patients "*sleep too little*" (yes/no) and use of hypnotics (yes/no). The distress of daytime symptoms; sleepiness, mental tiredness, physical tiredness and exhaustion were scored on a five point scale from no problems (1) to very big problems (5). The questionnaire also contains demographic questions about sex, age, marital status and employment situation. A modification by Edéll-Gustafsson and co-workers (2006) contained an explanation of the five-point scoring; *never*="never or less than once a month" (1), *seldom*="less than once a week" (2), *sometimes*="1-2 days a week" (3), *often*="3-5 days a week" (4) and *very often*="daily or almost daily" (5)[93].

When the questionnaire was used in the uremic population, questions about disturbances at sleep onset regarding uremic symptoms were added to the questionnaire[94]; leg creeping and pruritus scored never (1) to very often (5). In addition, treatment modality and treatment related problems were assessed; How often does your PD-machine alarm, is your sleep disturbed by the dialysis catheter or the dialysis solution? The answers were scored from "every night" (1) to "almost never" (5). The USI version from 2006 was the one used in this thesis.

Short Form (SF)-36

Health status i.e. health related quality of life (HRQoL) was assessed by a generic questionnaire, Short Form-36 (SF-36) (**III, IV**)[95]. The questionnaire consists of 36 items divided into eight health domains; physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role limitations due to emotional problems (RE) and mental health (MH).

All domains scores 0-100 where "0" represents the worst HRQoL and "100" the best[96]. The eight domains are dichotomised in two principal components; physical (PSC) and mental (MSC) component summary index.

International Restless legs Scale (IRLS)

The International Restless Legs Study Groups´ validated questionnaire, International Restless Legs Scale (IRLS)[97] evaluates the severity of RLS symptoms (**III, IV**) referring to the last week. The IRLS is a ten-item scale with a score ranging from 0-40. It is a ten item, five-point scale scored from "none" (0) to "very severe" (4) symptoms. The index scoring is divided in four groups of severity: negligibly (0-10), moderate (11-20), severe (21-30) and very severe (31-40)[97]. This questionnaire was not filled in by the CAD-patients and the population group in study **III**.

Sleep diary

During one week periods self-reported data of current sleep were collected by a study-specific sleep diary (**I, III, IV**). The sleep diary, completed day by day, yielded an overview of the patients´ sleep history. The sleep diary was used as data (**I, III**) and for controlling the agreement to the achtigraphy registrations (**III, IV**)[98]. The diary incorporated the same questions in all studies (**I, II, IV**) and was created with support from literature[99, 100] and the authors´ own experience from clinical work with PD-patients. To facilitate the responding for the patients the questionnaire was divided into one yellow (morning) and one blue (evening) sheet of

paper to fill in. Questions answered in the morning were; bedtime, sleep onset latency and number of nocturnal awakenings. Questions answered in the evening were; final morning awakening time, number and duration of napping and daytime symptoms i.e. sleepiness, physical tiredness, mental tiredness and exhaustion. Nocturnal sleep duration was calculated from the reported data.

FACIT-fatigue scale

Fatigue was measured in study **I**, **III**, and **IV** by Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale first developed for anaemic cancer patients[101]. The 13-item scale scores from "none" (0), to "very severe" (4) and the scale range is 0-52. The questionnaire includes items about tiredness, weakness and problems carrying out daily activities and refers to disease related and functional fatigue[79]. The cut-off score for fatigue is 43 or below and a value of 22 is two standard deviations below the cut-off, which is considered as severe fatigue[79]. This questionnaire was not filled in by the CAD-patients and the population group (**III)**.

Interviews

In study **II** the interviews aimed to obtain concrete and detailed descriptions of experiences from patients who have lived through situations of decreased sleep quality. The descriptions provided by the patients aimed to be as faithful as possible to the lived-through experience. Before the interview the patients were informed about the focus of the study and the situation to describe was selected by the patients following an open ended question by the researcher[102], *"Can you describe a day after you have had a bad night´s sleep"*. The patients had the chance to speak freely while the interviewer listened with attentiveness and openness and deepened the understanding through follow-up and clarifying questions such as; *"could you tell me more about…", "What do you mean by that?"*[102]. After the transcription the first interview was examined in detail in the research group to obtain improvements in interview performance.

Eleven interviews were carried out at the hospital and three at the patients' home and lasted between 25-51 minutes. In agreement with the 14

patients all interviews were tape-recorded and transcribed verbatim. The author of this thesis (PY-U) performed nine interviews and a co-author in study **II** (MG) performed five.

Procedures

The author (PY-U) visited the six participating hospitals and established a contact with the PD-nurses who were also informed about the studies. The nurses worked at a surgery for patients with PD and had a good personal knowledge about each available patient. Eligible patients matching the inclusion criteria were identified by the PD-nurses. A written invitation was distributed by the PD-nurse who also distributed the study information to the patients (**I-IV**). In study **I** the PD-nurse distributed the questionnaires and a stamped envelope to the patients during a routine appointment. Within 1-2 weeks PY-U contacted the patients by phone in case of questions about the study. In study **II** the PD-nurse also helped to find potential patients for interviews according to the inclusion criteria and made the first invitation along with written information. Thereafter PY-U or MG contacted the patients in case of questions and for making an appointment for the interview. In study **III** and **IV** the patients was included one-by-one owing to the availability of the study equipment. Thereafter the patients who agreed to participate were included in the study. Questionnaires and actigraphs were sent by post. Flowchart of the inclusion procedure is shown in figure 6.

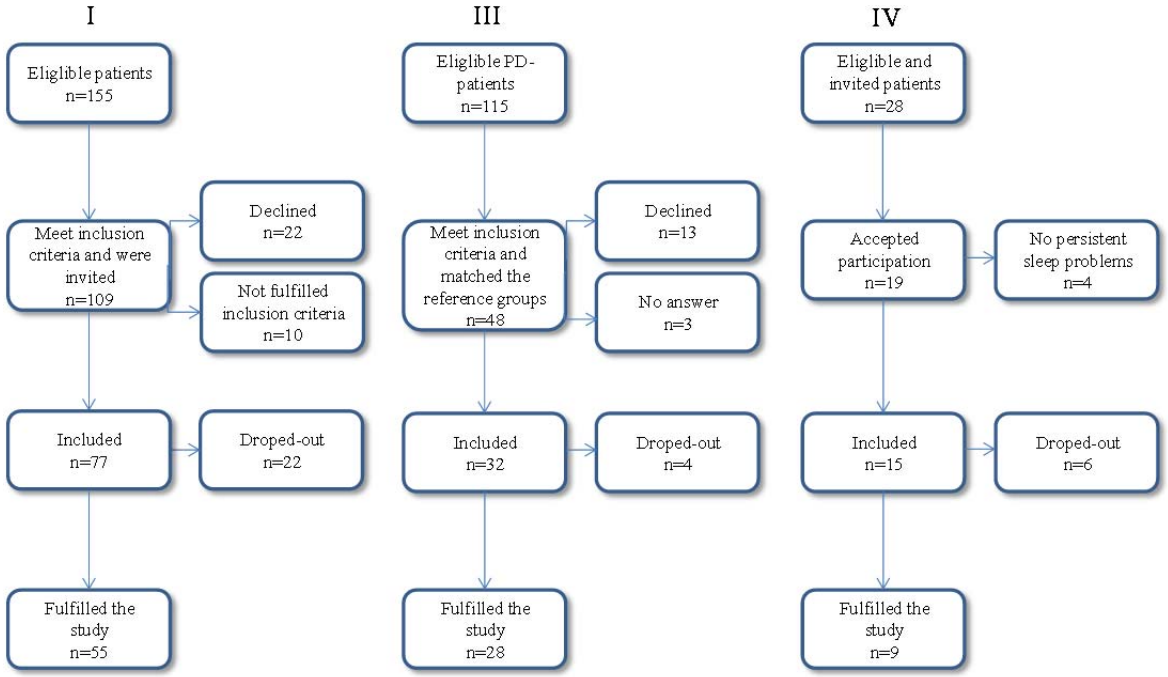

*Figure 6. Flowchart of the inclusion process for the PD-patients in study **I**, **III** and **IV**.*

Interventions

The 17-week nurse-led intervention study (**IV**) was separated in 5 phases, illustrated in Figure 7.

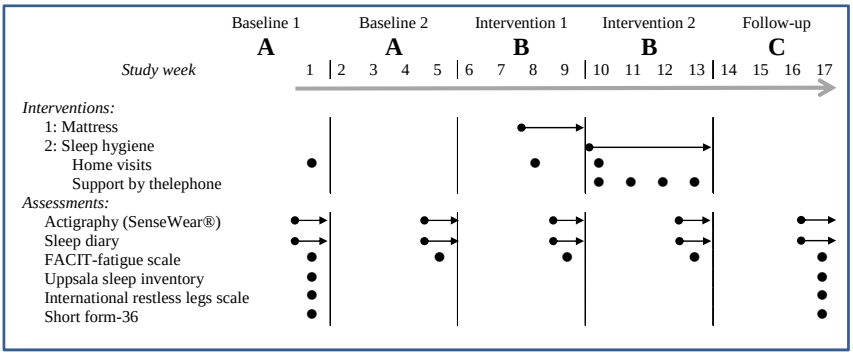

Figure 7. The study design with the study phases AABBC, shows the flow for the patients in the five study phases and the time points for intervention and data collection.

The two interventions were conducted separately and in two phases. After the two baseline measurements the first intervention was implemented. All participants were scheduled for a two-week intervention using a mattress (Tempur®) made by polyurethane foam which was delivered by PY-U to their homes. This intervention aimed to evaluate if the difficulties to find a comfortable sleep position could be reduced and increase the sleep quality since this was a problem previously detected (**I**) by our research group. The second intervention was an individual sleep hygiene and sleep scheduling programme. The baseline data were carefully analysed and formed the basis for the individually designed advice. Sleep habits and sleep related lifestyles together formed a set of rules which may be sleep promoting[63] i.e. sleep hygiene. The advice on sleep hygiene included reducing disturbing noises from the dialysis machine by for examples wearing ear plugs and increased physical activity during the day such as walking, gardening or light exercise. Stretching or light exercise before bedtime were also recommended since those activities can promote RLS[103]. It was also recommended that beverages containing caffeine were

to be avoided as caffeine has been suggested to be a predictor for RLS in patients on dialysis[104] and may impair sleep onset[105].

Regular sleep habits were established by sleep schedules. Through a regular sleep behaviour sleep efficiency can be increased when the sleep drive is built up by spending less time sleeping during daytime and going to bed and waking up around the same time every day[63]. Bright light therapy (Sunrise system 320® Bright LED portable light box, 10.000 Lux) was recommended in the morning for 30-45 minutes for correction of misaligned sleep-wake phases. This light was applied at a 30-50 centimetre distance to inhibit the internal secretion of melatonin[106]. The light box was delivered by PY-U to the patients' home. The numbers of sleep promoting recommendations were limited to no more than three for each patient (Table 3).

To evaluate the intervention effects nine outcome variables were selected: Sleep latency onset, Nocturnal sleep duration, Napping time, Number of naps, Sleep efficiency, Number of steps, MET (Kcal/Kg/hour), MFI and Fatigue. In addition individual health profiles from first baseline and follow-up were evaluated.

Table 3. Treatment plan with identified sleep problem, treatment goals, sleep hygiene applied, unexpected incidents and other symptoms of relevance for each patient A-I.

Patient /Diagnosis	*Sleep problems*	*Sleep intervention goals*	*Outdoor activity for minimum 30 minutes per day.*	*Sleep restriction: max. 30 minutes and before 3 pm.*	*Go to bed earlier, when sleepy*	*Go to bed later*	*[a]Bright light therapy in the morning*	*Ear plugs*	*No coffein after 6 pm*	*[d] Unexpected incidences during the study* *[e] Other symptoms*
A, Male:75 yrs Hypertensive nephropathy, Nefrectomy due to neprolihiasis Ichemic heart disease CAPD 48 month	Fragmented sleep with several naps	Consolidate nocturnal sleep Reduced freq. and time napping. Increased activity (steps, Metabolic Equivalent Unit (METs))	X	X						[e] Joint pain in lower extremity and esophageal dysfunction
B, Male: 76 yrs Unspecified renal disease Diabetes mellitus type II Multiple myeloma Coxarthrosis Heart failure CAPD 11 month	Too early morning awakenings, daytime sequelas and frequent napping	Consolidate nocturnal sleep Reduced freq. and time napping. Increased activity (steps, METs)	X	X		X				
C, Male: 74 yrs Diabetes mellitus type I with renal complications Nephrosclerosis Atrial fibrillation CAPD/APD 16 month	Delayed sleep phase, short sleep duration, fragmented sleep and daytime sequelas	Replaced sleep phases, Reduced freq. and time napping		X			X			[d] Severe infection and surgery at the lower extremity after the first intervention
D, Female: 47 yrs Polycystic kidney disease Hypertension Hyperlipidemia Epigastralgia CAPD/HD once a week 30 month	Sleep onset difficulties, Delayed sleep phase. RLS	Reduce nocturnal sleep duration Replaced sleep phases, Reduced freq. and time napping.	X[f]	X						[d] Serious social incident after first intervention
E, Male 77 yrs Glomerulonephritis MGUS+light-chain deposition disease APD 84 month	Sleep onset difficulties, nocturnal awakenings	Improve sleep onset Consolidate nocturnal sleep Increased activity (steps, METs)	X	X						[e] Joint pain in lower extremity
F[b], Male 48 yrs Polycystic kidney disease CAPD/APD 9 month	Sleep onset difficulties due to noise from PD-machine and daytime sequelas and work in a reduced light environment	Improve sleep onset Consolidate nocturnal sleep					X	X		
G[c], Female: 73 yrs Unspecified renal disease CAPD 15 month	Nocturnal awakenings and daytime sequelas	Consolidate nocturnal sleep Reduced freq. and time napping. Increased activity (steps, METs)	X	X						[d] Family incident after first intervention
H[b], Male 55 Diabetes mellitus type I with renal complications CAPD 4 month	Sleep onset difficulties, nocturnal awakenings related to RLS	Improve sleep onset Consolidate nocturnal sleep	X[f]						X	
I[c], Male 64 yrs Hypertensive nephropathy Polycystic kidney disease Asthma Heart failure CAPD 4 month	sleep onset difficulties, with daytime sequelas, and daytime napping	Improve sleep onset Consolidate nocturnal sleep Reduced freq. and time napping. Increased activity (steps, METs)	X	X	X					

[a]= Sunrise system 320® Bright LED portable light box – up to 10.000 Lux. Applied 30-45 min at 30-50 cm distance. [b]= Declined to use the mattress [c]= Removed the mattress after two nights, [f]= Sedentary activities before bedtime aiming to reduce RLS

Data analysis

Data was analysed according to the design and methods.

Statistical analyses

Descriptive statistics are presented as per cent (%), frequencies (n), mean (m) standard deviation (SD), median (Md), confidence interval (CI) and inter quartile range (Q_1-Q_3) when appropriate (**I, III**). In study **IV** data is presented graphically in accordance to the design of single-case studies with each patient represented over a timeline[107].

Non-parametric statistics were used when data was assessed on interval level, nominal scale or not normally distributed[108]. The variation between the days in the week, measured by the sleep diary (**I**) and the evaluation of the intervention effects (**IV**) was calculated with Friedman´s test. Between group statistics were calculated with Kruskall-Wallis test (**III**). Post-hoc test for Friedman's test was performed using Wilcoxon signed rank test (**I, III, IV**) and for the Kruskall-Wallis test Mann-Whitney U-test was used (**I, III**). Dichotomous variables were analysed using the Chi-square test (**III**). Spearman's rank order correlations coefficient (*r*) was used to explore associations between variables (**III**). The internal consistency was calculated with Cronbach´s alpha, at the three index scales; SF-36, IRLS, FACIT-fatigue (**III**).

To avoid reflections of normal fluctuations of the outcome variables in study **IV** a change of more than half a standard deviation was assumed to be clinically significantly[109]. All calculations were performed individually for each patient.

To explore the sleep quality two multiple linear regression analyses (forward procedures) were performed using *sleep variables*; sleep onset latency, nocturnal awakenings with difficulties to fall asleep again, sleep duration, too early morning awakenings, number of naps and *sleep disturbing factors*; pruritus, restless legs, difficulty to find a comfortable sleep position and nightmare as independent variables (**I**). The models demonstrated no multicollinarity problems since the highest observed variance inflation factor (VIF) was 1.5 and 1.9 respectively[110].

In the index scales, i.e. the questionnaires with a total summary score, missing data were handled through imputation of a mean or median substitution of the missing variable (**I, III**)[111]. To control the Type I error rate in the post-hoc tests a correction with Bonferroni was performed where a significant level was set to <0.016 (**III, IV**) and <0.007 (**I**) otherwise $p<0.05$ was accepted as statistical significant[111]. All statistical analyses were performed using the statistical software packages, SPSS 11.0-17.0 (**I, III**) and PASW 18.0 (**IV**). Microsoft Office Excel 2007 was used for graphs and statistical analyses (**IV**).

*Qualitative phenomenological analysis (**II**)*

Phenomenology is rooted in the philosophical tradition developed by Husserl and Heidegger. The phenomenological research design, based on Husserl's theory, was developed by Giorgi (1985) for systematically investigation in psychology[112] and has later been adopted into the field of nursing science. In this study the method aimed to describe the meaning of tiredness related to poor sleep in the way of the patients´ lived experiences i.e. to search for the essence of the phenomenon[102, 112]. The patients' description had a concrete everyday life perspective through the disciplinary perspective i.e. the perspective from nursing. The context in which the patients' made their expressions was also of importance for the analysis, which goes through four systematic steps[102, 113].

The first step was to read through the text to gain an understanding of the whole description. The second step was to establish meaning units. When sequences of the description have a change in nuances it was a start of a new meaning unit. Third step, the everyday language used by the patients was transformed to a professional language through a process of reflection and imaginative variation. Here the reduction started to take place. In the last step the determination of the situated structure was written down for each interview. To communicate the most general meaning of the phenomenon i.e. the essence, a general structure was achieved from all individual structures and was subsumed under one general structure[102]. During the analysis process the research group collaborated to obtain the structures from the data.

Both of the interviewers had several years of experience from patients with renal diseases and dialysis treatments. They also had theoretical and clinical knowledge about sleep problems in the same patient groups. In order to identify and be aware of their pre-understanding, ideas and knowledge of the phenomenon were written down. Before the interviews took place the interviewers worked closely together to ensure that the interviews were carried out in the same manner. Throughout the interviews and analysis previous understanding was put aside also known as bracketing. This meant to adopt openness and avoid engaging theoretical and previous knowledge in the interview situation or when data were analysed. The demand is to remain open to the data and of its contrary implications. This requires an attentively present to an ongoing experience told by the patients. This open attitude is also used in the analysis work[102]. All transcriptions and analyses work was made by PY-U.

Validity and reliability

The qualification "valid" is what separates science from other forms of knowledge, quantitative as well as qualitative methods. The degree of validity further refers to whether the conclusions in the study are correct[89]. In order to achieve validity in the quantitative studies (**I, III, IV**) all the questionnaires used for data collection had been tested psychometrically previously and had shown validity in other patient groups.

Validations between actigraphy and polysomnography have shown high sensitivity (89%) and specificity (95%) for diagnosing sleep apnoea[114, 115]. Furthermore, accuracy in number of nocturnal awakenings, awakenings after sleep onset, total sleep time and sleep efficiency in insomnia patients has been reported between actigraphy and polysomnography[116]. Both actigraphy and sleep diaries are methods of measurements in sleep research and in practice. The study specific sleep diary used in study **I-IV** was not a validated questionnaire but was created according to previously used models of sleep diaries[99, 100].

The USI questionnaire has been used in an epidemiological survey of a Swedish population[117] and has been examined in relation to polysomnography with strong resemblance regarding estimation of

difficulties falling asleep and sleep onset latency [118]. The USI has also been used in other chronic patients such as patients with coronary artery disease[99].

SF-36 is the most widely used generic questionnaire for evaluation of health outcome[95]. The scale has previously shown good reliability and validity[119, 120] with a Cronbach´s alpha between 0.79 and 0.91[119] and was in study **III** 0.75 in both PSC and MSC.

For IRLS the internal consistency reliability calculation showed a Cronbach´s alpha coefficient of 0.93-0.95[97] and 0.76-0.81[121]. In study **III** the Cronbach´s alpha coefficient was 0.95.

The FACIT-fatigue scale has been validated and showed a sensitivity of 0.92 and a specificity of 0.69[79]. The internal consistency showed a Cronbach´s alpha coefficient of 0.94[101] and was in study **III** 0.95.

Further, results from the questionnaires were in several variables confirmed by concurrent actigraphy registration. In study **IV** the interventions were evaluated by both subjective and objective outcome variables with well-established methods and validated questionnaires.

In qualitative research the "quality" of the research is often named as trustworthiness but according to the descriptive phenomenological method by Giorgi the method must comply with principles like; *systematic, methodical, general and critical*[113]. All four principles were considered trough all steps in the performance of the study (**II**). The systematic principle was to organise data in patterns, rather than randomly, and in some relation to each other. This is a part of the method and is also visualised in the model of the general structure (Figure 11, page 58). The use of an appropriate method in the scientific establishment is to be methodical. The general principle means that the knowledge has applications outside the specific situation, but is not the same as the highest form, generalisation. When the knowledge meets the critical members of the science society the structures, which are presented, should be judged by their outcome[113]. By using all of the available data and keeping the analysis close to the text, all the findings can be substantiated in the raw data[122].

The use of multiple methods, designs and measurements for interpretation about sleep and daytime symptoms (method triangulation) further enhancing the strength of the thesis[89].

Ethics

All studies were performed in accordance with the Declaration of Helsinki[123] and after approval by the Regional Ethical Review Board at the faculty of Health Sciences, University of Linköping. The patients were informed written and verbally before participation in all the studies and signed informed consent forms were obtained from all participants. None of the participants were in a dependent relationship to the investigator and all patients were able to decide to enrol the study by themselves. Withdrawal from the study could be done without explanations and did not interfere with normal treatment or care.

In all studies the participants were given a code name. The code-key was only available for the researcher and confidentiality was guaranteed. In study **II** the participants were informed that the interviews were tape recorded and verbally transcribed. Considerations regarding risks of emotional or psychological harms caused by interviews or questionnaires were taken in all studies. The participant was invited to contact the interviewer, or the PD-nurse in charge at the clinic, after the interview in case of need. The participants were also informed about how to contact the investigator (PY-U) in case of questions. In study **IV** non-pharmacological and non-invasive interventions were applied and recommended to the patients after medical consultation at the department of neurophysiology and in some special cases the physician in charge was informed. No risks were identified for the participants and all interventions were evaluated to be beneficial for the participants and to promote their health.

Results

SLEEP PROBLEMS WAS IDENTIFIED by use of achtigraphy, self-reported data and in interviews.

Prevalence of sleep problems

According to the definition of insomnia 60% (**I**) and 36% (**III**) of the participating PD-patients were categorised as insomniacs. The PD-patients identified as insomniacs scored significantly decreased sleep quality compared to non-insomniacs (**III**), md (Q1-Q3), 2 score (1.25-3.0) vs. 3 score (2.0-4.0), where a higher score indicates better sleep quality (Figure 8).

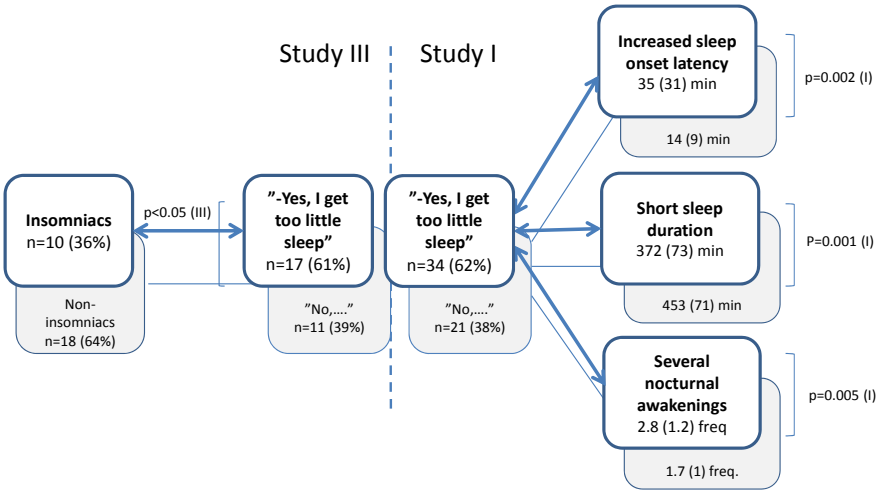

*Figure 8. Associations between PD-patients categorised as insomniacs and not insomniacs (shadowed squares) regarding sleep quality and decreased sleep variables presented in mean (SD) in study **I** (n=55) and study **III** (n=28).*

Furthermore, 61% (**III**) and 62% (**I**) gave an affirmative answer to the question; “do you get too little sleep?”, thus indicating a significantly impaired sleep compared to those who did not report too little sleep (Figure 8).

Disrupted sleep was identified in all of the PD-patients by actigraphy registration (**III**). None of them had an MFI below 20 whereas 11 (39%) had serious fragmentation, above 50 (Figure 9) this was significantly higher compared to the CAD-patients and the population group (**III**).

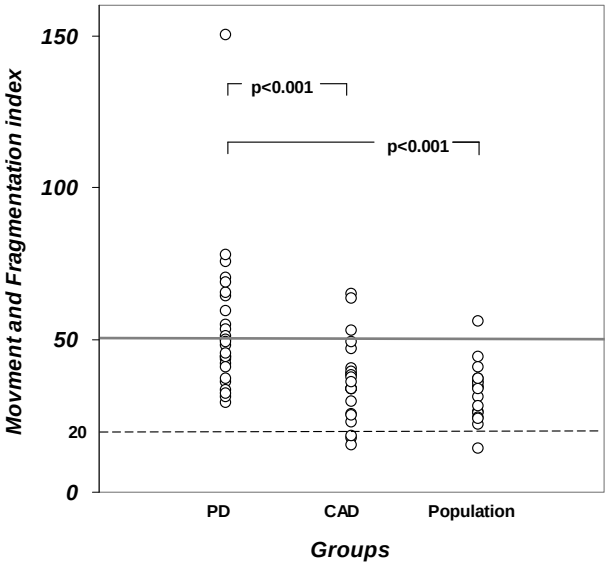

*Figure 9. Distribution of fragmented sleep in peritoneal dialysis patients (PD), Coronary Artery Disease (CAD) and the population group. Above 50 indicates much disrupted sleep and below 20 means well consolidated sleep (**III**). Reproduced with permission from the publisher.*

Mean frequency of wake bouts per night during the registration week was 32 (SD 27-36) measured with actigraphy, this was significantly higher than in the CAD-group (Table 4).

*Table 4. Group comparison of PD-patients in study **I** and **III** and patients with Coronary Artery Disease (CAD) and a population group from study **III**, between sleep variables assessed by actigraphy and a sleep diary during one week and the questionnaire Uppsala Sleep Inventory (USI) covering habitual sleep over 4 weeks.*

Sleep variables	PD-group n=28 (**III**) Md (Q_1-Q_3)	PD-group n=55 (**I**) Md (Q_1-Q_3)	CAD group (A) n=22 (**III**) Md (Q_1-Q_3)	Population group (B) n=18 (**III**) Md (Q_1-Q_3)	P-value (**III**) (Kruskal-Wallis)
Age (yrs)	60 (54-67)	66 (56-74)	62 (58-70)	60 (55-64)	
Sleep quality (score)					
1=bad, 5=very good	3 (2-4)**(A)	3 (2-4)	2 (1-3)	2 (1-4)	0.006
Sleep latency (min)					
Actigraphy	30 (22-59)***(B)	N.A.	24 (10-41)	13 (7-26)	0.002
Sleep diary	28 (16-75)***(**I**)	13 (5-22)	16 (12-34)	18 (9-34)	0.001
USI	25 (6-60)**(A)	33 (16-50)	10 (1-20)	10 (3-23)	0.007
Sleep duration (hour.min)					
Actigraphy	6.42 (5.58-7.17)	N.A.	6.50 (6.05-7.37)	6.43 (6.30-7.12)	0.903
Sleep diary	7.06 (5.54-8.00)	7.23 (6.19-8.02)	6.55 (6.03-7.25)	6.17 (5.50-7.05)	0.132
USI	7.00 (5.00-8.00)	7.07 (6.00-8.00)	7.00 (4.42-8.00)	7.00 (5.06-7.00)	0.951
Go to bed (time)					
Actigraphy	22:41 (21:41-23:04)	N.A.	22:55 (22:33-23:20)	23:03 (22:41-23:19)	0.079
Sleep diary	22:23 (21:29-22:55)	22.26 (21.41-23.11)	22:27 (22:00-22:56)	22:35 (22:27-23:03)	0.278
USI	22:00 (21:00-23:00)**(B)	22.30 (22-23)	22:00 (21:42-22:30)*(B)	23:00 (22:00-23:00)	0.009
Nocturnal waketime (min)					
Actigraphy	94 (70-122)**(A)***(B)	N.A.	64 (41-91)	58 (47-73)	0.001
Sleep diary	20 (8-52)	N.A.	24 (10-37)	21 (12-43)	0.973
USI[a]	4 (2-5)	4 (2-6)	3 (1-4)	4 (1-6)	0.056
Wake bouts (freq)					
Actigraphy	32 (27-36)**(A)	N.A.	26 (19-34)	24 (20-31)	0.051
USI	2 (1-3)**(B)	2 (1-3)	3 (1-4)*(B)	2 (0-2)	0.015
Nap time (min)					
Actigraphy	59 (39-92) **(B)	N.A.	48 (30-57)	32 (14-47)	0.009
USI	45 (10-60)***(**I**)	60 (30-79)	45 (11-60)	30 (11-60)	0.463
Fragmentation index[b]					
Actigraphy	49 (41-64) ***(A)(B)	N.A.	35 (25-42)	34 (26-37)	0.0001
Sleep efficiency[c] (%)					
Actigraphy	71 (68-80)**(A)***(B)	N.A.	78 (75-85)	83 (82-87)	<0.0001
USI		78 (67-91)			
Sleep Sufficient Index[d] (%)					
USI	80 (72-94)*(A)(B)(**I**)	93 (78-100)	93 (83-100)	93 (86-100)	0.027

(<0.016), ** (<0.01), * (<0.001) versus coronary artery disease (CAD) patients (A) general population (B) and the PD-patients in study **I**. Mann-Whitney U test adjusted with Bonferroni.*

[a] Score; <5 min (1), 5-15 min (2), 15-30 min (3), 30-60 min (4), 1-2 h (5), 2-3 h (6), >3 h (7) .[b]Movement and fragmentation index indicates restless and fragmented sleep; bad sleep (>50) and very good sleep (<20). [c] Sleep efficiency; below 85% indicates insufficient sleep efficiency .[d] Sleep Sufficient Index; below 80% indicates insufficient sleep sufficiency. Not Applicable (N.A.)

The patients´self-reported sleep efficiency (USI) was md 78% (Q_1-Q_3 67-91) (**I**) and in the actigraphy based calculation it was 71% (68-80) in study **III**. This was significantly lower compared to CAD-patients and the population group 78% (75-85) p<0.01 and 83% (82-87) p<0.001, respectively (**III**).

Prevalence of sleep disturbing factors

Moderate to very severe pruritus were reported by 50% (**I**) and 57% (**III**) of the patients and RLS by 47% (**I**) and 46% (**III**). Both pruritus and RLS were negatively associated to sleep variables and domains in SF-36 (Figure 10).

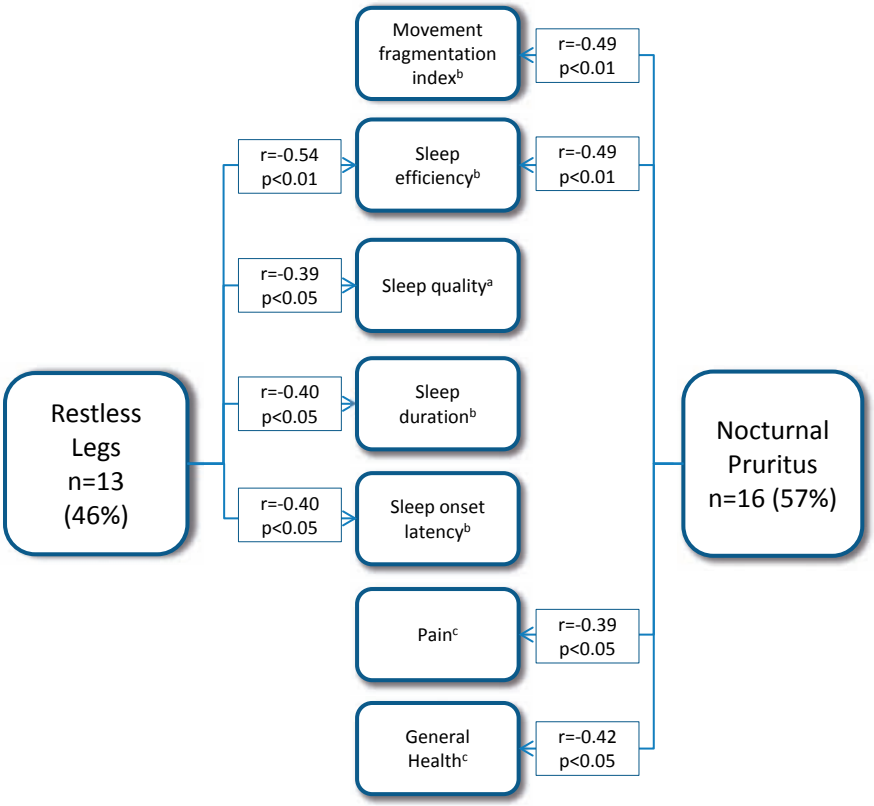

*Figure 10. Nocturnal pruritus and restless legs negatively correlated with sleep variables, measured by USI[a], actigraphy[b] and SF-36[c] (**III**).*

Nocturnal pruritus, difficulties to find a comfortable sleep position and nightmares were sleep disturbing and predictive factors for the sleep quality and explained the sleep quality with 56%, $p \leq 0.0001$ (**I**). Further sleep duration and nocturnal awakenings with difficulties to fall asleep again explained the sleep quality with 57% $p \leq 0.0001$ (**I**). Apnoeic behaviour was reported to 4% (**III**) and 15% (**I**).

Prevalence of daytime symptoms

Thirty-two percent (**I**) and 62% (**III**) of the PD-patients reported that their sleep not was refreshing (severe-very severe). Further, thirty-three percent (**I**) and 72% (**III**) of them also felt sleepy during the daytime. Physical tiredness 36% (**I**) and 76% (**III**) was more prevalent than mental tiredness 19% (**I**) and 24% (**III**). Sleepiness and physical tiredness were also the most prevalent daytime symptoms in CAD-patients, 61% and 56%, and in the population group, 56% and 38% (**III**). In addition fatigue was scored as very high by the PD-patients, 88% (**I**) and 89% (**III**) respectively and napping was reported as a frequently used behaviour 75% (**I**).

Experiences of poor sleep

The experiences of tiredness linked to poor sleep appear in one general structure, *circling around in tiredness* (**II**). The model consists of four parts, *sensations of being tired, need for sleep and rest, consequences in daily life* and *strategies for adjustments.* The sensation of being tired influences the experiences in the other three parts named constituencies and each of them contain variations (Figure 11). The structure is circular and is independent of a starting point. The structure can represent a day-to-day experience as well as an on-going process extended over time.

One way to describe the structure is that the tiredness experienced by the patients yields sensations in different parts of the body, both mentally and physically. Those sensations affect the experience of tiredness which is characterised by an increased need for sleep. Having sensations of tiredness affect everyday life activities, impair cognitive functions and

limit social activities. To handle the tiredness the patients became fighter, gave up or adjusted to the new conditions.

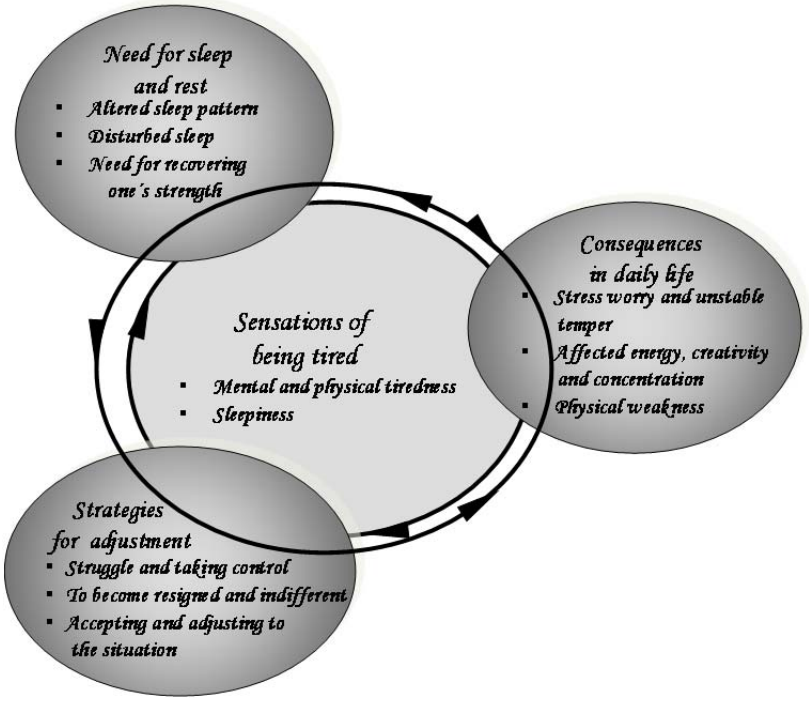

Figure 11. The structure," Circling around in tiredness", and the relation between the four parts ***(II)*** [124]*(pp 409). Reproduced with permission from the publisher.*

The sensation of being tired

Three variations were identified. *Mental and physical tiredness* was described as a part of the chronic disease. Mental tiredness dominated the physical sensations, which was an experience of weakness but not comparable with the desire to sleep. Inactivity enhanced the sensation of tiredness. *Sleepiness* was described as located in the mind, as feelings of unreality, drowsiness and a longing for sleep. Recovering from loss of deep sleep was harder. Sleepiness was easier to identify before bedtime compared to lack of sleep the day after a bad night´s sleep, which was more recognised as tiredness.

Need for sleep and rest

Behaviour with frequent nocturnal waking and daytime naps was a cumulative behavioural problem that was difficult to break because naps were a way of managing through the day and led to an *altered sleep pattern*. Broken sleep was experienced as a problem linked to uremic symptoms like RLS, pruritus, and to draining and refilling the dialysis solution as well as poor sleep positions. Furthermore, the night dialysis machine and nightmares could be disturbing. *Disturbed sleep* was not discussed with the health-care providers. Starting the treatment was described as a turning point with an increased need for recovering the strength. The alertness from the dialysis treatment was overshadowed by a new burden from self-care management. Capacity before the illness brought unrealistic expectations. Experiences of symptoms and pharmacological treatment brought an increased *need for recovering one´s strength* and a feeling of being lazy arose when they were resting.

Consequences in daily life

Due to the patients´ lack of sleep *stress, worry and unstable temper* were experienced. They described a needed to drop household tasks due to tiredness which contributed to stress. In sleep onset moments existential thoughts came up with worries about complications and death. The patients expressed a longing for more activity but the *energy, creativity and concentration were affected* and every task took longer to perform. After a good night's sleep it was easier to make decisions and they felt more motivated. A feeling of loneliness arose when the family carried on just as before. They experienced a gradual *physical weakness* and inability to rebuild physical strength was a circular problem. Discomfort and ungracefulness with the dialysis solution in the abdominal cavity contributed to a more sedentary lifestyle.

Strategies for adjustment

It was described that energy could be gained from actively thinking of a healthier period in life and tiredness and sleepiness could thus be dispelled.

They let the days pass as planned by *struggling and taking control* which was encouraged by the health-care providers. Sleep was described as a way to escape and passive activities such as watching TV were adopted. Passivity contributed to sleep problems when they spend more time sleeping during daytime and their joy disappeared when they thought of their former health, they *become resigned and indifferent.* Others described how they *accepted and adjusted to the situations* by taking advantage of micro-breaks, adopted a slower tempo or made no promises to participate in activities in case of lacking energy.

Effects of a non-pharmacological intervention programme

The results of the non-pharmacological intervention programme showed that three of the nine participating patients (*B, G, I*) improved clinically significantly in five or more of the nine outcome variables measured in the end of the last intervention phase compared to baselines (Figure 12).

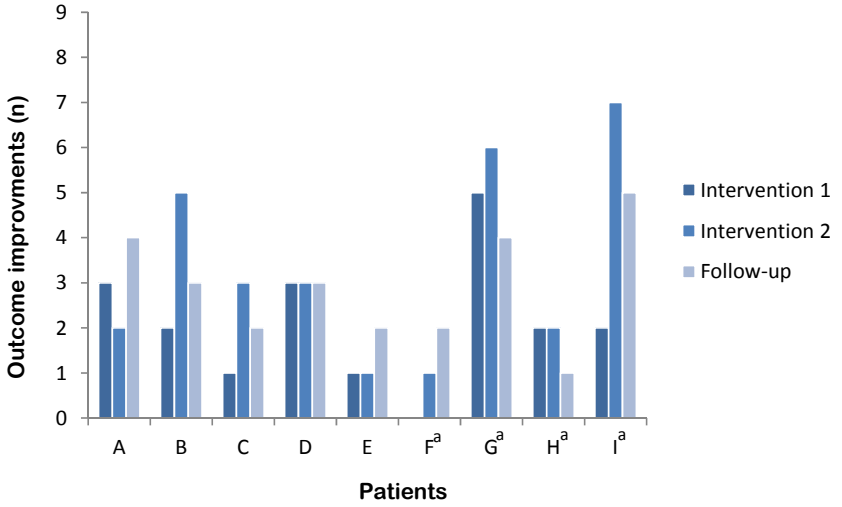

Figure 12. Number of clinically significantly individual outcome improvements at intervention 1 (mattress) and intervention 2 (sleep hygiene) compared to baseline (=0). Patients B, G and I improved clinically significantly in five or more of the nine variables during intervention 2. For more details se study ***IV****.* [a]*=declined use of the mattress.*

Three of the patients (*F, G, I*) increased nocturnal sleep duration, decreased napping time (Figure 13) and improved number of steps and METs clinically significantly.

Four of the patients *(A, G, H, I)* statistically significantly improved sleep efficiency and three (*A, D, I)* decreased nocturnal fragmentation (MFI) (Figure 13). Two of the three youngest patients were above the cut off score for fatigue in study phase 4. At the follow-up the patients were clustered in two groups, one group around the cut off score 43 and the other around two standard deviations (score 22) below the cut off and one of them, *C*, had scored below five. Assessment of health profiles were performed at the first baseline and at the follow-up. The three youngest patients (*D, F, H*) had the widest area which indicates a better self-reported health both at baseline and at follow-up. Further the health status reflects a severe infection and surgery in patient *C* after the first intervention. The other patients had low self-reported health at baseline and at follow-up (Figure 14).

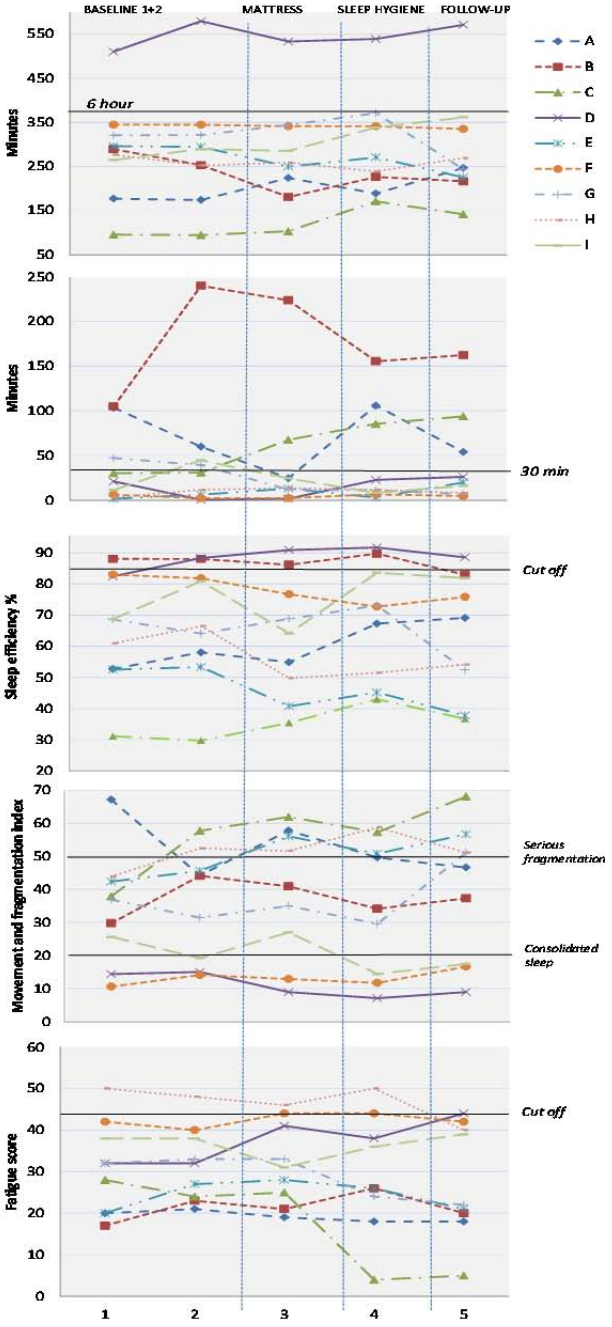

Figure 13. Visualisation of nocturnal sleep duration, napping time. Changes in sleep efficiency and movement and fragmentation index (MFI) and fatigue score in patient A-I during the five study phases.

Recommendations in persistent insomnia: Nocturnal sleep duration >6 hours and daytime napping <30 minutes.

Sleep efficiency more than 85% and MFI below 20 are well consolidated sleep. MFI above 50 indicates seriously disrupted sleep.

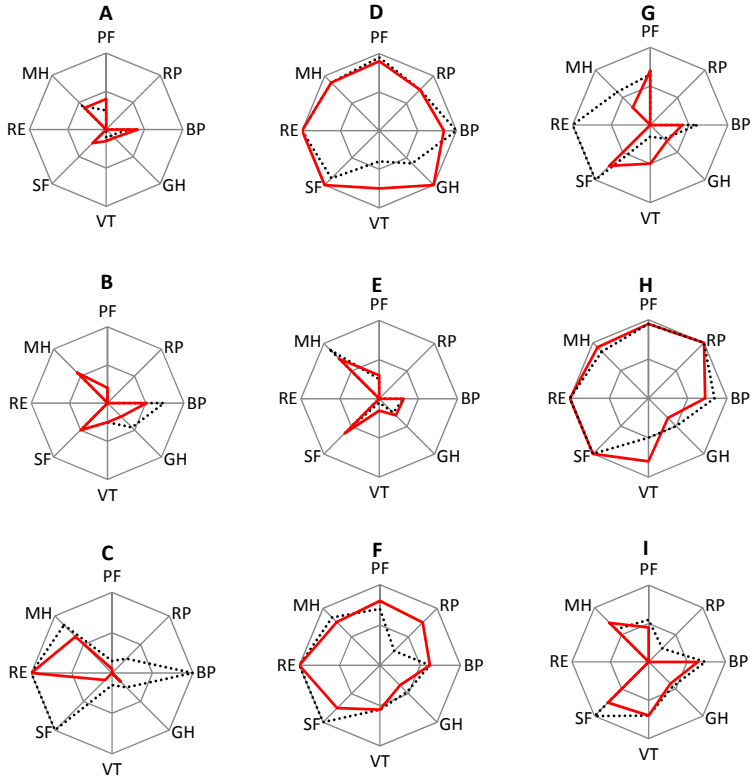

Figure 14. Health profiles (SF-36) from baseline 1 (dotted line) to follow-up (red line) in patient A-I. A narrow area indicates poor health and a wide area indicates good health. PF=physical functioning, RP=role limitations due to physical health problems, BP=bodily pain, GH=general health, VT=vitality, SF=social function, RE=role limitations due to emotional problems and MH=mental health. Scale: 0 (centre)-100.

General discussion

THE FOCUS OF THIS THESIS WAS TO DESCRIBE, sleep problems from different perspectives, and how these problems affect daily life and health in patients treated with peritoneal dialysis at home. The objective was also to evaluate a non-pharmacological intervention for improvement of sleep quality outcomes. The main findings showed that PD-patients had seriously fragmented sleep and a high prevalence of insomnia. Sleep was mainly disturbed by pruritus and by RLS. Daytime impairments and a frequent napping behaviour were detected and in addition a high prevalence of fatigue was reported. The patients described that an ever-present tiredness and poor sleep had consequences for their everyday life physically, mentally, socially and existentially.

The intervention study demonstrated that a nurse-led individual, non-pharmacological, sleep intervention could improve sleep and daytime activities in PD-patients.

Sleep problems

In study **II** the patients described that the illness and the dialysis treatment was a turning point for increased need for recovery, which has previously only been described in a population with mixed dialysis modalities[125]. This phenomenon was mirrored by the sleep sufficient index (ratio of time in bed divided by presumed sleep) in study **III** which was significantly lower in the PD-patients than in the CAD- and the population groups but also significantly lower than in the PD-patients in study **I**. The difference from study **I** may be explained by a significantly longer sleep latency onset, and shorter sleep duration in the patients in study **III**.

The prevalence of insomnia was found to be high, 60% (**I**) and 36% (**III**). The discrepancy in frequency of insomnia is unclear since the same

measurement and criteria for insomnia were used in both studies. The discrepancy may be explained by the patients in study **I** being older and more patients reporting apnoeic behaviour in study **I**. Persistent sleep problems have previously been reported to vary between 60-89% in PD-patients[126, 127]. In general populations the prevalence is lower 9.5-15%[128, 129]. Despite having been described as a prevalent problem, in dialysis populations the definition for insomnia used in the studies[39, 40] is unclear. The definition requires both nocturnal and daytime problems[46]. Consequently the whole 24-hour period is important to assess which also is supported by the descriptions by the patients in study **II**. In study **IV** all participants were categorised as insomniacs but demonstrated a variety of problems, since the definition of insomnia contains early, middle and late insomnia along with daytime symptoms[46]. In a clinical situation sleep problem needs to be thoroughly explored to prescribe the most appropriate treatment. This will be discussed in clinical implications on page 77.

The PD-patients showed a seriously fragmented sleep, 39% had a fragmentation index above 50, which was statistically significantly higher compared to the CAD- and the population groups (**III**). In study **IV** four of the nine patients had above 50 in the MFI. The present finding, with a high MFI may explain the low sleep efficiency, poor sleep quality and the frequency of symptoms experienced during the day since fragmented sleep reduces the restorative deep sleep as well as the amount of sleep time[130]. The higher fragmentation in PD-patients compared to the CAD-patients and the population group may be caused by a higher prevalence of sleep disturbing factors i.e. pruritus and RLS. The discrepancy between the self-reported and actigraphy registered wake-bouts (**III**) illustrates the fact that the fragmentation is unconscious micro-arousals[131] and must be objectively assessed.

Although, dialysis treatment decrease the uremia and uremic symptoms the patients still are in an inflammatory condition[132]. Accordingly, poor sleep quality can intensify the inflammatory condition[133] which is important to consider since infections and cardiovascular diseases are the two most prevalent causes for death in dialysis populations[1].

The results also showed that 57% of sleep quality outcome could statistically significantly be explained by nocturnal awakenings with difficulties falling asleep again and short sleep duration (**I**), which is new knowledge not previously published.

Sleep disturbing factors

The most common sleep disturbing factor detected in this thesis was pruritus with a prevalence of 50% (**I**) and 57% **(III**). This was also one of the three independent variables that explained the sleep quality by 56% (**I**) which is also new knowledge. The aetiology of uremic pruritus is probably multifactorial and a attempts to classify uremic pruritus from the level of its origin in the path from the ends of the distal C-fibres to cortex has failed due to its complexity[134]. Pruritus has earlier been described as a prevalent symptom in dialysis patients, 40-55%[11, 135] supporting the relationship between pruritus and mortality in haemodialysis patients[135]. In study **III** pruritus correlated to the sleep variables MFI and sleep efficiency. Sleep fragmentation and reduced sleep efficiency can in this thesis partly be addressed to nocturnal pruritus as it has been confirmed in dialysis populations previously where patients disturbed by pruritus had significantly more time awake during the night, $p<0.002$[52]. Consensus about reliable tools for assessing such a prevalent and disturbing symptom as uremic pruritus is lacking.

Another potential sleep disturbing factor is RLS which affected 47% (**I**) and 46% (**III**) of the patients. The results are in analogy with previously studies where RLS was reported to affect 8-52% of a mixed population with dialysis and pre-dialytic patients[11] and 47-62% of PD-patients[126, 136]. Study **III** also showed associations between RLS and sleep efficiency, sleep quality, sleep duration and sleep onset latency. This was not surprising since RLS affects sleep as symptoms worsen in the evening or during the night[49]. RLS has showed a statistically significantly higher arousal index (fragmentation), measured by polysomnography, in ESRD patients compared to ESRD patients without symptoms of RLS[137]. No significant correlation to MFI was found but such an association has been

described previously[137, 138]. RLS in dialysis patients has further shown associations with decreased physical function, decreased well-being and even an increased mortality risk[47] which can partly be explained by the decreased sleep quality that comes with symptoms of RLS.

Apnoeic behaviour was self-reported by the patients and affected 4% (**III**) and 15% (**I**). This is lower than in other studies with uremic patients where a tenfold higher prevalence has been reported (57%)[139] but higher compared to people with normal renal function were the prevalence was 2-4%[130]. Both of those studies have used polysomnography for evaluation of apnoea which is more accurate than questionnaires since this behaviour is difficult to self-report. Episodes of hypoxemia are a result of sleep apnoeic behaviour and mostly an arousal to which the patient is unconscious. In treatment with nocturnal HD it has been suggested that the obstructions in the upper airways might be caused by oedema and that a central apnoea can be related to central destabilization, respiratory control[140, 141] and acidosis which were improved by nocturnal dialysis[141]. Fragmented sleep with hypoxemia caused by sleep apnoea is an alarming problem in peritoneal dialysis patients and a serious risk for fatal cardiovascular incidences[142, 143]. It is important to keep in mind that apnoea, RLS and pruritus can induce fragmented sleep or insomnia, either separately or in combination. In addition depression has been pointed out as a predictor for poor sleep in patients with chronic kidney disease[144]. Therefore symptom evaluations are essential since the clinical picture is complex.

Sleep related daytime symptoms

Severe daytime symptoms varied between 18-76% (**I, III**), where physical tiredness was the most frequent, 36% (**I**) and 76% (**III**) followed by sleepiness 33% (**I**) and 72% (**III**). The discrepancy between study **I** and **III** is unclear but in study **III** 46% of the PD-patients reported a regular use of hypnotics compared to those in study **I** where only 18% used hypnotics. This difference may be explained by the fact that daytime sleepiness is a common side effect.

The prevalence of fatigue was reported to be extremely high 88-89% (**I**, **III)** and similar results have been identified in dialysis populations in previous studies, 55-97%[74, 145]. Despite the high prevalence of fatigue, this symptom is often ignored by both patients and health-care providers. This can partly be explained by the fact that both health-care providers and patients attributed the symptoms of fatigue to the disease itself (**II**). This point of view was also reflected in the interviews with the patients where they described an increased need for rest and also decreased energy and abilities to concentrate and be creative (**II**). This description corresponds to the definition stated by Cella and co-workers used in this thesis "*…diminished energy and mental capacity and increased need to rest…*"[79] (pp 528). An association between fatigue and sleep disorders has also been suggested in patients with chronic kidney disease[78, 146, 147] and in dialysis patients with lack of physical activity[146]. There is also evidence for substantial impact of fatigue on sleep in other chronic diseases i.e. Sjögrens´s syndrome and rheumatoid arthritis[148]. Study **III** further showed a correlation between fragmented sleep and fatigue, this is new knowledge regarding PD-patients. This correlation supports results from another study that described excessive sleepiness or fatigue can be independent consequences of sleep disorders. This hypothesis was built from results on patients with diagnosed insomnia, who had normal subjective sleepiness but reported severe fatigue[149]. This study further suggested that fatigue may be an earlier indicator than sleepiness for sleep loss if the drive to sleep is mild to moderate[149]. Since the FACIT-fatigue scale essentially assesses functional fatigue the high prevalence of fatigue reported by the PD-patients can therefore, partly be addressed to a decreased physical function[146].

Another clinical report showed that the majority of patients with chronic insomnia reported inability to sleep during the day despite having the opportunity to do so[150]. Perceptions of sleepiness can be masked or minimised by excitement, motivation or physiological needs such as hunger. Fatigue, on the other hand, is relatively unaffected by a stimulating environment[149]. Longtime sleepiness may also be underreported owing to habituation[149, 151]. This means that patients who experience their sleepiness

as normal will be more unlikely to seek medical help[151]. This demonstrates the difficulty in the assessment of sleepiness and fatigue.

As a consequence of decreased sleep quality, tiredness, mood changes, reduced ability for show initiative and to staying concentrated was described by the patients (**II**). This can be understood as cognitive disabilities that may also be affected by contributing factors like the chronic illness itself and difficulties related to the uremic state and the treatment. Clinical effects from pruritus have been shown; 61% of patients with ESRD had difficulties to fall asleep and 36% reported to be more agitated[152] which probably also can be explained by decreased sleep quality caused by pruritus. An experimental study on healthy individuals with sleep restrictions showed that the participants underestimated their self-reported cognitive impairment and overestimated their performance[153]. Furthermore, low cognition function scores have been reported in dialysis patients with persistent sleep problems[154] and that cognitive impairments could be covered by trying harder in performance[64]. In a situation with an extended responsibility for self-care management it is of importance to gain or maintain cognitive functions as the safety of the treatment management can otherwise be endangered e.g. in the exchange of dialysis solutions.

Napping was a frequently used behaviour in the PD-patients (**I**) and may be a way to manage daytime sleepiness attributed to fragmented sleep. The PD-patients further took statistically significantly longer naps than the CAD-patients and the population group in study **III**.

Extended naps, lasting more than 30 minutes, can be an awakening from slow-wave sleep. Awakenings in this sleep stage are characterised by confusion, grogginess and decreased performance i.e. sleep inertia[155]. Symptoms from sleep inertia could be misinterpreted as fatigue and vice versa since fatigue is characterised as diminished energy and mental capacity and an increased need for rest[79]. In the interviews the patients confirmed an increased need for rest and daytime napping behaviour (**II**) as well as an overall lower activity, measured by actigraphy. This was statistically significantly lower in the PD-patients compared to the CAD-patients and the population group (**III**). Besides decreased sleep quality a

reduced physical function may contribute to more rest which can result in daytime sleep.

Non-pharmacological treatments

Based on study **I, II**, and **III** an intervention study was designed which aimed to evaluate effects of non-pharmacological interventions on sleep, activity, fatigue as well as reduction of sleep disturbing factors (**IV**).

Three of the nine included patients with insomnia symptoms stopped or reversed a progression of negative sleep behaviour by sleep hygiene advice. Moreover, improvements were also seen in the other six patients. The results have to be considered as positive since this is a group of multi-disease and frail patients. Although the patients did not reach the recommended sleep duration of six hours they may have benefited from their improved sleep.

Increased physical activity was prescribed for all of the patients who succeeded to improve five or more of the nine outcome variables and they succeeded to achieve a clinically significantly increase in METs and number of steps. Whether the increased activity or the exposure for daylight contributed to improvements is not possible to decide. Interestingly, it has been reported that increased physical function measured in a group of haemodialysis patients showed improved sleep quality[61].

Only one of the nine patients had a sleep duration longer than the minimum recommendation of six hours (**IV**)[156]. During the intervention and the follow-up two patients decreased napping time significantly to maximum 30 minutes. One patient succeeded both reduced napping time and increased nocturnal sleep duration. A well-established restriction limits the naps to no more than 30 minutes and not later than 3.00 pm for insomniacs[60]. This recommendation is mostly useful for increasing the nocturnal sleep. However, there are results that implicate that napping time contributes to the total amount of sleep during a 24-hour period[157] and should consequently not always be reduced. This implication is important to consider when prescribing daytime sleep restrictions to PD-patients.

Sleep efficiency measure the amount of time in bed that is actually spent sleeping. This is an important variable and was significantly improved in five of nine patients (**IV**). Sleep fragmentation was clinically significantly improved in three of the patients and reached values below 20. This is an essential improvement from the intervention since fragmented sleep reduces the restorative deep sleep i.e. sleep quality with metabolic[158] and immunologic[70, 159] alterations.

Four patients improved in fatigue score, but only one who improved in five or more variables also improved in fatigue. This finding is not fully understood. One explanation can be a delay in the experience of decreased fatigue or that an extended period of improved sleep is needed to reduce a persistent symptom like fatigue. This explanation does not support the theory by Hossain and co-workers that fatigue is an early detector of increased need for sleep[149]. On the other hand fatigue can also be a result of other disease-related factors i.e. uremia or a persisting inflammatory condition[132] which can also be intensified by decreased sleep quality[133].

Three patients (*G, H, I*) who did not use the mattress improved outcomes during this intervention phase. In this study phase there had been no sleep education or advice. This may be explained by the increased attention from the researcher but also from the patient´s own awareness of sleep behaviour initiated by questions from the researcher when the sleep history data was obtained. Therefore it is difficult to evaluate the outcome of the mattress.

This study indicates that non-pharmacological treatment for insomnia can be a treatment of choice for PD-patients (**IV**). Behavioural treatments for insomnia have demonstrated advantages on other frail individuals and people in late life and have been reported to sustain the sleep quality over time. Hypnotics did also improve the sleep quality but was only effective in the short term[60]. Regarding side-effects from hypnotics PD-patients may even be frailer since, for examples drug metabolism often is altered. Therefore a non-pharmacological treatment for sleep problems may be preferred.

Methodological considerations

The strength in this thesis is that objective data from more than 700 sleep-wake cycles were collected in home environments. In addition a variation of qualitative and quantitative study designs were used.

Samples

There were a relatively high number of drop-outs in the studies and the respondent rate for participants was 60% (**I**), 58% (**III**) and 60% (**IV**). As a comparison, in a health survey study among healthy Danish individuals, the respondent rate for a self-administered questionnaire declined from 68% in 1994 to 51% in 2005[160]. So, the respondent rates among available patients in study **I, III** and **IV** are acceptable since the patients' health was poor and they had high prevalence of fatigue.

The sample sizes in study **I** and **III** can be considered as small and therefore generalisation must be implemented carefully. However, the results are in congruence with previously research and the samples represent 6.6% (**I**) and 3.3% (**III**) of the Swedish national PD-sample. Nine patients fulfilled the single-case study (**IV**) which is a relatively large sample for this type of design. Single-case designs has adopted the primary principle for empirical generality that is *replication*[107]. A single-case study is therefore unusually conducted on just one single subject[107] making each case a replication of the first one. The 14 participants in study **II** were selected based on a variation regarding patient characteristics. This sample can be considered as large in a phenomenological study. Giorgi states; "*The more subjects there are, the greater the variations, and hence the better the ability to see what is essential. On the other hand, specific situated structures might still be desired and these could be based on only one subject.*"[112] (pp.19).

Methods

The assessment of RLS in study **I** was based on a question from USI. The question refers to "leg creeping" which is considered equal to RLS.

The prevalence was similar to the prevalence found in study **III** where the valid IRLS was used in combination with actigraphy, described as a valid and reliable method to detect RLS[138].

The study specific sleep diary used in all of the quantitative studies (**I, III, IV**) was not a validated questionnaire. However, the formulation of the questions was adopted and inspired from the literature and referred to time points for sleep variables e.g. bedtime. No indications in misconceptions of the questions have been found in the studies. In another study with cancer patients a high degree of congruence has been found between actigraphy and sleep logs except for number of nocturnal awakenings[161].

To evaluate sleep polysomography is still the golden standard. But, there are some advantages with actigraphy registration i.e. the whole sleep-wake cycle can be evaluated in the home environment for several days, activity parameters are registered and the device can be applied easily by the patients. One study has showed that the night-to-night variability is high and records of just one night´s sleep does not reflect normal sleep patterns[162]. However, one disadvantage can be that sleep is indirectly measured since motionless periods are measured as sleep and periods of movements as wakefulness. This could imply that actigraphy overestimates sleep latency onset and may not be used as a single diagnostic tool.

The interventions were performed according to the principles of self-care management where the patients were educated about sleep and were instructed and taught how to manage their individual sleep problems. Moreover, the Hawthorne effect i.e. the increased attention from the researcher (**IV**) might be considered as bias[163]. On the other hand, the coaching by the first author might have been an important intervention in itself. This effect has been used from in other self-care interventions, in telephone case management following heart failure admission[164] and in PD-patients to control symptoms, prevent complications and promote lifestyle by weekly supportive phone calls[164, 165]. Both of those studies showed positive clinical outcomes.

To succeed with sleep hygiene advice was not only about the power of the intervention i.e. sleeping hygiene or giving the right advice. It was more about finding a way to motivate and educate the patients who realised to the practical modifications in daily life. Therefore the intervention design was comparable to a clinical situation since the role of the researcher was supportive and educative according to the assumptions in renal supportive care. Another effect is nurse-dose effect that refers to the amount of nurse time and number of contacts with the patients. This effect has been associated with decreased morbidity, mortality and healthcare costs[166] which can also be useful in a clinical situation.

Further limitations might be that some of the components in cognitive-behavioural therapy (CBT), which is standard in primary insomnia[59], were excluded. The reason was that most of the sleep problems in the PD-population could be referred to sleep disturbing factors which can be defined as secondary insomnia. Furthermore, to acquire a new behaviour or lifestyle might need more than four weeks of intervention period. The outcome variables were strictly following sleep parameters and no data regarding motivation and coherence were obtained which can be a limitation. The high mortality rate, in the dialysis population, 26.1% (range 21.2-29.7%)[1] is a limitation for extended study plans and long-term follow-ups.

Analysis

Several statistical analyses were performed and statistical methods were chosen and performed, appropriate to the data i.e. sample size, data level and normal distribution of the variables.

The internal consistency (Cronbachs´ alpha) of the questionnarrie was recalculated and compared with the original testing. The internal consistency was acceptable for SF-36 (PSC: 0.75 and MSC: 0.75) but on the border of being too high in IRLS (0.95) and the FACIT-Fatigue (0.95) (**III**). This may indicate that some of the questions were too similar. However, this indication was noticeable even at the original development of the scales[97, 101] and has so far not resulted in an elaboration of the scales which could eventually result in a reduction in the number of items on the

scale. The impact of the high internal consistency on results is probably negligible.

In a single-case study design the focus is not on performing statistical calculations on a group level therefore data were interpreted at an individual level and each patient served as their own control. Individual changes of half a SD have been suggested to be clinical significant [109] which can be considered as a rough calculation. However, normal individual fluctuations can be reduced and each patient can be evaluated individually. This method was applied in study **IV**. Another author has suggested that differences of less than half a SD can be considered as clinically significant[167]. After calculations, of health related quality of life data, Norman and co-worker suggests that the minimal important difference is 0.3 rather than 0.5[168]. Since there are no consensus half a SD is a reasonable and scientifically estimation of a meaningful effect size[169]. In a group design averages in outcome variables will be unlikely to represent a single individual with multifaceted problems and will therefore not be very helpful in a clinical situation. But, the generality of a particular behaviour or phenomenon confirmed by a single-case study can be discussed. However the experimental criteria based on a comparison of behaviour under different conditions i.e. intervention and nonintervention phases is fulfilled as well as the criteria for replication[107, 170].

The strength in study (**II**) is the faithful application of Giorgi´s descriptive phenomenological research design and the compliance with the four principles of validity according to the phenomenological method[112, 113, 122]. Throughout the interviews and the analysis researchers strived for openness and awareness of the pre-understanding of the phenomenon; which is called "bracketing"[102, 113]. A qualitative researcher does not seek to generalise the findings. Nevertheless transferability is not appraised to be inadequate and the findings might be useful for a wider understanding e.g. in hemodialysis patients[102, 112].

Ethical reflections

The principles of the declaration of Helsinki were applied in all studies. Participating in a study requires contribution from the patients. The

respondent burden was small in study **II**, where interviews were conducted. In study **I** and **III** a battery of questionnaires were supposed to be filled in during the week of actigraphy registration, which might have been a burden for the respondents. Study **IV** called for greater efforts in the interventions and a kind of cooperation were established with the patients. As a researcher it was important to be responsive to the patients and to facilitate distributions of equipment as far as possible. Even the frailest patients who suffered complications during the study period were very eager to complete the study. The outcomes from the interventions were considered positive and were hopefully perceived as beneficial for their sleep and daytime symptoms.

Clinical implications

Assessment, treatment and evaluation of sleep problems and tiredness belonging in the field of healthcare providers' responsibility and nephrology nurses are in a unique position to identify patients with these problems. The patients described self-care management activities, developed by themselves. Some activities were counterproductive activities i.e. using sleep as a way of escape during daytime and some were rational self-care activities i.e. by taking advantages of micro-breaks and adopt a slower tempo. However, the healthcare providers were not described by the patients as being engaged in the problems (**II**).

The healthcare providers can respond to the patients' strategies in different ways. One way can be to encourage a struggling patient as a "good patient" which may not always be productive. For some patients, energy saving activities might be promoted instead.

According to Nobles[19] renal supportive care is not only related to end of life treatment but rather related to the care at all stages of renal illness[19]. In their definition of palliative care the WHO also give some recommendations that are suitable in dialysis care, "…to provide relief from…distressing symptoms", "enhance quality of life", "positively influence the course of illness", "treatment early in the course of illness in conjunction with other therapies that are intended to prolong life"[171].

Applying those recommendations in the care for PD-patients can mean to prevent, identify and assess symptoms. Furthermore, it can mean to provide support in self-care management and treatment to enhance quality of life early in the care, even before the start of the dialysis treatment.

Identifying problems

PD-patients need skills for self-care and treatment management, which include intellectual functions, cognitive functions, responsibility, compliance and psycho-physiological health. Those functions can be impaired by sleep problems[64, 67].

Healthcare providers should regularly assess sleep history and daytime performance as the PD-patients´ prevalence of sleep problems is high[94, 172, 173]. In study **II,** conducted in a Swedish cultural context, "tiredness" was the expression that referred to sleepiness, tiredness as well as fatigue. Therefore healthcare providers must be sensitive to what symptom the patient refers to and more specific questions are needed[174]. In addition, indications of daytime sleepiness, reduction in activity and inappropriate naps should initiate an individual sleep examination. It is also easier for healthcare providers to be attentive to visible symptoms[175] which is important to consider since sleepiness, tiredness and fatigue cannot always be observed during an out-patient visit. Furthermore, a positive answer to the dichotomous question "do you get too little sleep" may indicate sleep problems since too little sleep showed statistically significant longer sleep-onset latency, shorter sleep duration and more frequent nocturnal awakenings (**I**) and should initiate further examinations.

Assessment

The results in this thesis are based on both self-reported and objective assessments can be implicated for assessment of sleep problems in clinical work[176]. Since sleepiness and fatigue can be produced by impaired sleep but are different manifestations the conditions also need separate assessments. Suggestions to inquire about sleep on a regular basis and to distribute appropriate questionnaires during out patients visits has been proposed in elderly individuals[177]. In figure 15 a sleep assessment process

is proposed from this thesis in order to identify and collect data to support diagnosis and treatment, some steps may be omitted since the assessments are individualised. Sleep problems are an interdisciplinary concern[19] and any professional with a broad knowledge and understanding of sleep-wake problems in the dialysis team may initiate and lead the process.

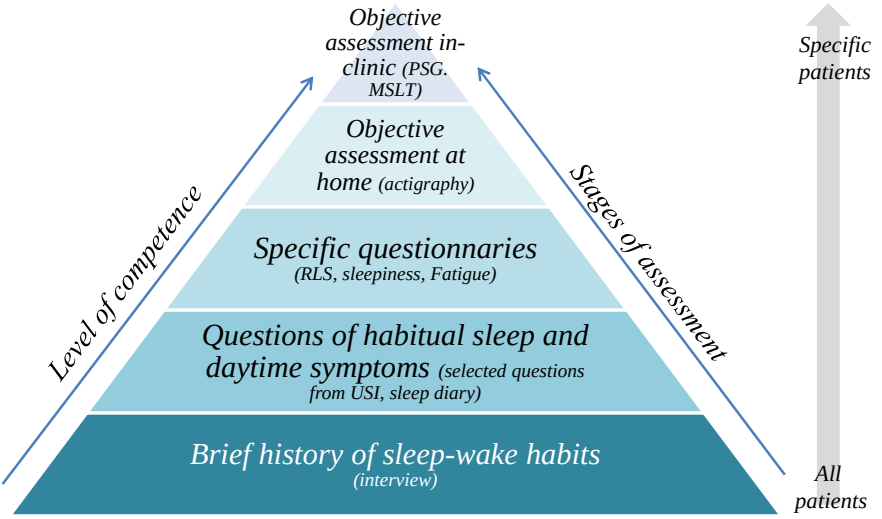

Figure 15. Stages of assessment in sleep-wake problems. USI=Uppsala Sleep Inventory, RLS=Restless legs, MSLT=Multiple Sleep Latency Test, PSG= Polysomnography.

Treatments

The symptom management model by Dodd and co-workers has been suggested to be generalisable[176] and can be used to understand the results from this thesis and has also been elaborated with implications from the theory of unpleasant symptoms[13] in this thesis. *First*, the model suggests individual assessment with both a history of the sleep problem and appropriate questionnaires[176]. The patients have an opportunity to express perceptions of the symptoms such as, intensity, distress, duration and quality[13]. It may be useful to help the patients explore their experience through questions such as; "compared to what?" since older patients have shown a decreased awareness in somatic symptoms[174]. *Second*, identify a

focus for the treatment intervention, with a broad approach directed to more than one of the problems since symptom can be clustered and since sleep problems is not the only problem affecting daytime function. Symptom burden are numerous[11] and co-existing problems such as symptoms of depression can interfere with sleep[178]. *Finally*, the intervention should be specified as to what will be intervened, when to intervene, the "dose" of the intervention and the way it will be managed [176]. More intensive interventions strategies for other symptoms than those related to sleep problems also have to be considered. The treatment process, adopted from Morgan & Closs[100] and elaborated in this thesis, is displayed in figure 16.

In addition the positive outcome from the nurse-dose (or any other profession) intervention[166] may contribute to a positive outcome. This treatments may not restore sleep completely, but may probably improve sleep quality[179] which can contribute to a reduction of the total symptom burden and conversely a reduced symptom burden may improve sleep, which was demonstrated in three patients in study **IV**.

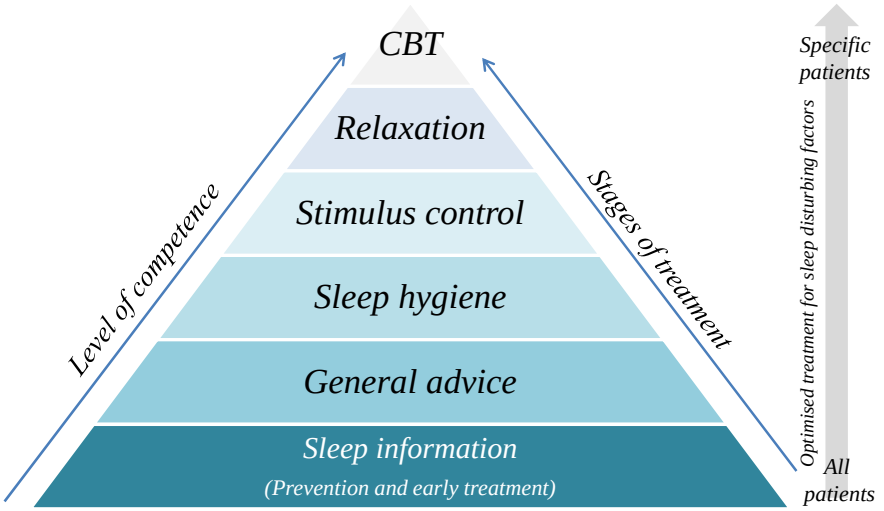

Figure 16. Stages of non-pharmacological treatment approach, modified and elaborated from Morgan and Closs[100] related to competence and treatment process. CBT=Cognitive Behavioural Theraphy

Future directions

In future research it seems to be important to further investigate sleep problems i.e. insomnia in PD-patients as a 24-hour disorder. However, the high MFI also requires investigations of other possible sleep fragmenting factors i.e. sleep apnoea or factors interfering with sleep in other ways, like depression and drug therapy. Furthermore, there is a lack of knowledge on how disturbed sleep interferes with cognitive impairments and self-care management abilities in PD-patients. More intervention studies are also warranted with extended designs regarding both time for the interventions as well as more combinations of treatment options i.e. combining non-pharmacological and pharmacological sleep therapies. Furthermore, research regarding the impact of biochemical alterations in uraemia and of the dialysis treatment on sleep quality and sleep regulation is warranted.

Summary and conclusions

BASED ON THE RESULTS ACHIEVED IN THIS THESIS the major findings are:

- Sleep problems categorised as insomnia were highly prevalent in a Swedish PD-patients population.
- Pruritus and restless legs was the most prominent sleep disturbing factors.
- As measured with actigraphy registration, sleep was seriously fragmented, in PD-patients and also associated with pruritus. The fragmentation was significantly higher in PD-patients compared to CAD-patients and a population group.
- Sleep quality was explained by nocturnal pruritus, difficulty to find a comfortable sleep position, nightmares, nocturnal awakenings and sleep duration.
- Tiredness related to poor sleep is described by the patients to have consequences in many dimensions of everyday life; physically, mentally, socially and existentially.
- The most frequent daytime impairment was fatigue.
- Napping was a frequently used behaviour.
- The whole 24-hour period is of importance for assessing sleep behaviour and daytime functioning i.e. sleep-wake cycle.
- Individual and non-pharmacological sleep hygiene interventions improved sleep behaviour and daytime activity in PD-patients.

Sammanfattning

SÖMN PROBLEM ÄR VANLIGT FÖREKOMMANDE, 49-86%, hos patienter som behandlas med peritonealdialys (PD). Insomnia d.v.s. svårigheter att inleda och/eller upprätthålla sömnen eller ett för tidigt morgonuppvaknande, i kombination med symtom dagtid, är ett av de vanligaste problemen. Trots den höga prevalensen hos PD-patienter är problemet otillräckligt beforskat. I synnerhet saknas studier med objektiva datainsamlingsmetoder och studier som undersöker hela dygnet. Det saknas också studier som utvärderar interventioner av icke-farmakologisk behandling av sömnproblem i denna patientgrupp.

Avhandlingens övergripande syftet var att beskriva sömnproblem ur olika perspektiv och hur dessa problem påverkar det dagliga livet och hälsan hos patienter som behandlats med PD i hemmet. Syftet var också att utvärdera om ett individualiserat icke-farmakologiskt behandlingsprogram kunde förbättra sömnkvalitet och minska dagsymtom.

Fyra studier har genomförts under åtta år med början 2002. Patienter från sex sjukhus i sydöstra Sverige inbjöds att delta i studierna. Datainsamlingen genomfördes med självrapporterade frågeformulär, actigrafiregistrering och intervjuer. I en av studierna jämfördes också PD-patienter med två referensgrupper; kranskärlssjuka och befolkning. I interventionsstudien (single-case design) utvärderades effekten av individualiserad sömnhygieniskrådgivning med stödjande telefonsamtal.

Sammanlagt har data från 700 dygn inhämtats. De viktigaste resultaten visar tydligt att PD-patienter har en allvarlig fragmentering av sömnen även jämfört med kranskärlssjuka och befolkningsgruppen. Resultatet visade också att ett stort antal PD-patienter kunde klassificeras enligt kriterier för insomnia. Sömnen var främst störd av klåda och restless legs (RLS). Funktionsnedsättningar dagtid som sömnighet, mental och fysisk trötthet samt utmattning var frekvent rapporterat och resulterade i tupplurar

hos ett stort antal patienter. Prevalensen av fatigue (långvarig trötthet) rapporterades också vara extremt hög 88-89% hos PD-patienter. I intervjustudien beskrevs en ständigt närvarande trötthet och en försämrad sömnkvalitet som gav konsekvenser i det dagliga livet både fysiskt, mentalt, socialt och existentiellt. Den individanpassade icke-farmakologiska interventionen, baserad på sömnhygien, visade att både sömn och dagsymtom kan förbättras.

Avhandlingen visar att störd sömn är mycket vanligt hos PD-patienter och att fragmenterad sömn resulterar i dagsymptom och fatigue. Med stödjande omvårdnad, en systematisk bedömning och en individualiserad icke-farmakologisk behandling kan sömnkvalitet och fysisk aktivitet hos kroniskt sjuka patienter med peritoneal dialys förbättras.

Acknowledgements

I WOULD SINCERELY LIKE TO EXPRESS MY gratefulness to all of you, who in different ways, contributed to my work with this thesis.
I would especially like to thanks;
All **patients,** who have been so helpful and collaborative.
Ulla Edéll-Gustafsson, my supervisor, for introducing me to the world of science and sleep research. You believed in my project idea from the start and did not give up despite periods of lack of resources in the projects.
Anders Fernström, my co-supervisor for your encouraging, positive and supportive attitude, for always being available by e-mail and for competently corrected my writing and letting the red ink flow.
Sussanne Börjeson, my co-supervisor and boss, you have generously shared your experiences and knowledge with me and helped me to see more and new perspectives in my work. You allowed me to think and not only produce research.
Martin Magnusson, for your contribution, together with my co-supervisor Anders, for my re-employment at my former place of work, the department of nephrology, as a financial support.
Maria Friedrichsen, co-author, for being an invaluable support in qualitative methods, you have encouraged me to open the door slightly to the world of phenomenology.
Anna Johansson, co-author, thank you for support, friendship and fruitful cooperation. Good luck with the final spurt of your thesis.
Professor emeritus; **Anna-Christina Ek,** for accepting me as a doctoral student and for advice and discussions about single-case research. Thank you for help and support when I needed it.
Maria Gustavsson, co-author, for cooperation and help with the interviews in the Kalmar area.

Matthias Alvunger, for collaboration with the department of medicine at Kalmar hospital.

To the PD-nurses at the participating clinics for help with recruitment of the patients; **Berith Boo, Helena Eriksson, Karin Berggren, Anna Hallberg-Karlsson, Birgitta Lundberg, Annika Tuvedsson, Marianne Fagerström, Anette Karlsson-Perebom, Inger Eriksson, Anette Strömberg, Eva Ekström, Annelie Ljungdahl-Jonsson** and **Andreas Lägermo.**

Lindy Gustavsson for excellent proofreading and language corrections.

Sofia McGarvey for practical and administrative assistance, always available with quick replies and for excellent proofreading.

Helena Folin, for invaluable help with statistical transformation of my problematic "time-data".

Olle Eriksson, for statistical discussions and advice.

All **PhD-students** at the division of nursing science; Tanks for fruitful discussions at seminars, constructive criticism and relaxing and tasty coffee breaks. Special thanks to my friends and colleagues **Katarina Berg, Birgitta Salomonsson, Lena Näsström** and **Eva Molander** for listening and being supportive in moments of frustration.

Division of neurophysiology; Professor **Eva Svanborg**, for your competent advice on sleep research and for allowing me use your softwear program for free. **Martin Ulander**, for your generous support in sleep management and actigraphy registration and **Per Hammarlund** for technical support.

Åsa Källstrand-Thor for help with graphic design in paper II.

Jenny Betmar, librarian, for help and support with EndNote.

My past and present **colleagues** at the department of Nephrology and the division of nursing science and the nursing programme, for showing genuine interest in my work with this thesis.

My dearest friends, the **Olinder, Berg-Karlsson and Thörnqvist** families, our "big parties" and after-works counterbalanced the hard work and helped me to slow down. The "book-club", with **Britta, Emma** and **Maria,** gave me breaks to read something else but research and discuss literature and everything else between heaven and earth.

My dear parents **John** and **Gulli Yngman** for loving me and caring about me and my family, and for providing practical support not least with construction work in our home.
My sister **Anna** for always being available for debriefing of any kind and to her husband **Anders** and their lovely daughters **Nora** and **Ellen**.
My passed away grandmother **Stina**, I miss our phone calls! If I reach your age I have plenty of time to produce a lot of research.
Last in my list but in the first place in my heart, my closest family. My beloved husband **Fredrik,** for always believing in me, even when I doubted, thank you for supporting, loving me and caring about me. Our lovely children **Rebecca** and **David,** you gave me what was most important…a life beyond this thesis. I love you all so much!

Thanks to you all!

Pia

Financial support was granted from; Ingrid Asp foundation, Research Council of South-East of Sweden (FORSS), Swedish Kidney Association (RNj), Swedish Match foundation (Solstickan), The Swedish Research Council, Swedish Sleep Research Association (SFSS), Ulrica Cronés foundation, Department of Nephrology, County Council of Östergötland and Linköping University.

References

1. SNR. Svenskt Njur Register. 2009 [cited 2011-03-02]; Available from: http://www.medscinet.net/snr/rapporter.aspx
2. ISPD. The emergence of Peritoneal Dialysis. 2011 [cited 2011-03-15]; Available from: www.ispd.org/media/pdf/genesis.pdf
3. Doolan PD, Murphy WP, Jr., Wiggins RA, Carter NW, Cooper WC, Watten RH, et al. An evaluation of intermittent peritoneal lavage. Am J Med. 1959; **26**(6): 831-44.
4. Thomas N, editor. Renal Nursing. 3 ed. London: Bailliére Tindall, Esevier; 2008.
5. Palmer RA, Quinton WE, Gray JE. Prolonged Peritoneal Dialysis for Chronic Renal Failure. Lancet. 1964; **1**(7335): 700-2.
6. Popovich RP, Moncrief JW, Nolph KD, Ghods AJ, Twardowski ZJ, Pyle WK. Continuous Ambulatory peritoneal Dialysis. Annuals of International Medicine. 1978; **88**: 449-56.
7. Diaz-Buxo JA, Farmer CD, Walker PJ, Chandler JT, Holt KL. Continuous cyclic peritoneal dialysis: a preliminary report. Artif Organs. 1981; **5**(2): 157-61.
8. Boen ST. Overwiev and history of peritoneal dialysis. Dialysis and Transplantaion. 1977; **6**: 12-8.
9. Stel VS, van de Luijtgaarden MW, Wanner C, Jager KJ. The 2008 ERA-EDTA Registry Annual Report-a precis. NDT Plus. 2011; **4**(1): 1-13.
10. Lindqvist R, Carlsson M, Sjoden PO. Perceived consequences of being a renal failure patient. Nephrol Nurs J. 2000; **27**(3): 291-7; discussion 8.
11. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. Adv Chronic Kidney Dis. 2007; **14**(1): 82-99.
12. Weisbord SD, Fried LF, Arnold RM, Fine MJ, Levenson DJ, Peterson RA, et al. Prevalence, severity, and importance of physical and emotional symptoms in chronic hemodialysis patients. J Am Soc Nephrol. 2005; **16**(8): 2487-94.
13. Lenz ER, Pugh LC, Milligan RA, Gift A, Suppe F. The middle-range theory of unpleasant symptoms: an update. ANS Adv Nurs Sci. 1997; **19**(3): 14-27.

14. Riegel B, Weaver TE. Poor sleep and impaired self-care: towards a comprehensive model linking sleep, cognition, and heart failure outcomes. Eur J Cardiovasc Nurs. 2009; **8**(5): 337-44.
15. Curtin RB, Johnson HK, Schatell D. The peritoneal dialysis experience: insights from long-term patients. Nephrol Nurs J. 2004; **31**(6): 615-24.
16. Morton RL, Devitt J, Howard K, Anderson K, Snelling P, Cass A. Patient views about treatment of stage 5 CKD: a qualitative analysis of semistructured interviews. Am J Kidney Dis. 2010; **55**(3): 431-40.
17. Berzoff J, Swantkowski J, Cohen LM. Developing a renal supportive care team from the voices of patients, families, and palliative care staff. Palliat Support Care. 2008; **6**(2): 133-9.
18. Germain M, Cohen LM. Renal supportive care: view from across the pond: the United States perspective. J Palliat Med. 2007; **10**(6): 1241-4.
19. Noble H, Kelly D, Rawlings-Anderson K, Meyer J. A concept analysis of renal supportive care: the changing world of nephrology. J Adv Nurs. 2007; **59**(6): 644-53.
20. Chow SK, Wong FK. Health-related quality of life in patients undergoing peritoneal dialysis: effects of a nurse-led case management programme. J Adv Nurs. 2010; **66**(8): 1780-92.
21. Sadala ML, Miranda MG, Lorencon M, de Campos Pereira EP. Nurse-patient communication while performing home dialysis: the patients' perceptions. J Ren Care. 2010; **36**(1): 34-40.
22. RNJ. Guidelines for the care of kidney patients. 2005 [cited 2011-02-11]; Available from: http://www.njurforbundet.se/Njurförbundet_Riktlinjer%20och%20studiehandledning.se.aspx
23. Kryger M, Roth T, Dement W, editors. Principles and practice of sleep medicine. 4 ed. Philadelphia: Elsevier Saunders; 2005.
24. Carney P, Berry R, Geyer J, editors. Clinical sleep disorders. 1 ed. Philadelphia: Lippincott Williams & Wilkins; 2005.
25. Orzel-Gryglewska J. Consequences of sleep deprivation. Int J Occup Med Environ Health. 2010; **23**(1): 95-114.
26. Ohayon MM, Bader G. Prevalence and correlates of insomnia in the Swedish population aged 19-75 years. Sleep Med. 2010; **11**(10): 980-6.
27. Yoon IY, Kripke DF, Youngstedt SD, Elliott JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. J Sleep Res. 2003; **12**(2): 87-93.
28. Dijk DJ, Groeger JA, Stanley N, Deacon S. Age-related reduction in daytime sleep propensity and nocturnal slow wave sleep. Sleep. 2010; **33**(2): 211-23.
29. Elmenhorst EM, Elmenhorst D, Luks N, Maass H, Vejvoda M, Samel A. Partial sleep deprivation: impact on the architecture and quality of sleep. Sleep Med. 2008; **9**(8): 840-50.

30. Knutson KL, Van Cauter E. Associations between sleep loss and increased risk of obesity and diabetes. Ann N Y Acad Sci. 2008; **1129**: 287-304.
31. Koch BC, Nagtegaal JE, Hagen EC, Wee PM, Kerkhof GA. Different melatonin rhythms and sleep-wake rhythms in patients on peritoneal dialysis, daytime hemodialysis and nocturnal hemodialysis. Sleep Med. 2010; **11**(3): 242-6.
32. Borbely AA, Achermann P, Trachsel L, Tobler I. Sleep initiation and initial sleep intensity: interactions of homeostatic and circadian mechanisms. J Biol Rhythms. 1989; **4**(2): 149-60.
33. Broughton RJ. SCN controlled circadian arousal and the afternoon "nap zone". Sleep Res Online. 1998; **1**(4): 166-78.
34. Atkinson G, Davenne D. Relationships between sleep, physical activity and human health. Physiol Behav. 2007; **90**(2-3): 229-35.
35. De Vecchi A, Finazzi S, Padalino R, Santagostino T, Bottaro E, Roma E, et al. Sleep disorders in peritoneal and haemodialysis patients as assessed by a self-administered questionnaire. Int J Artif Organs. 2000; **23**(4): 237-42.
36. Yang JY, Huang JW, Peng YS, Chiang SS, Yang CS, Yang CC, et al. Quality of sleep and psychosocial factors for patients undergoing peritoneal dialysis. Perit Dial Int. 2007; **27**(6): 675-80.
37. Eryavuz N, Yuksel S, Acarturk G, Uslan I, Demir S, Demir M, et al. Comparison of sleep quality between hemodialysis and peritoneal dialysis patients. Int Urol Nephrol. 2008; **40**(3): 785-91.
38. Kurella M, Luan J, Lash JP, Chertow GM. Self-assessed sleep quality in chronic kidney disease. Int Urol Nephrol. 2005; **37**(1): 159-65.
39. Merlino GP, A. Dolso, P. et. al. Sleep disorder in patients with end-stage renal disease undergoing dialysis theraphy. Nephrol Dial Transpl. 2006; (21): 184-90.
40. Sabry AA, Abo-Zenah H, Wafa E, Mahmoud K, El-Dahshan K, Hassan A, et al. Sleep disorders in hemodialysis patients. Saudi J Kidney Dis Transpl. 2010; **21**(2): 300-5.
41. Jansson-Frojmark M, Linton SJ. The course of insomnia over one year: a longitudinal study in the general population in Sweden. Sleep. 2008; **31**(6): 881-6.
42. Ohayon MM, Sagales T. Prevalence of insomnia and sleep characteristics in the general population of Spain. Sleep Med. 2010; **11**(10): 1010-8.
43. American Psychiatric Association. Diagnostic criteria from DSM-IV-TR. Washington, D.C.: American Psychiatric Association; 2000.
44. WHO. International statistical classification of diseases and related health problems. 10th revision, 2nd edition. ed. Geneva: World Health Organization; 2004.

45. American Academy of Sleep Medicine. The international classification of sleep disorders : diagnostic and coding manual. 2nd ed. Westchester, Ill.: American Academy of Sleep Medicine; 2005.
46. Socialstyrelsen. Sick leave for insomnia 2010 [cited 2011-02-15]; Available from: http://www.socialstyrelsen.se/riktlinjer/forsakringsmedicinsktbeslutsstod/insomni
47. Unruh ML, Levey AS, D'Ambrosio C, Fink NE, Powe NR, Meyer KB. Restless legs symptoms among incident dialysis patients: association with lower quality of life and shorter survival. Am J Kidney Dis. 2004; **43**(5): 900-9.
48. Patrick LR. Restless legs syndrome: pathophysiology and the role of iron and folate. Altern Med Rev. 2007; **12**(2): 101-12.
49. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med. 2003; **4**(2): 101-19.
50. Horvath J, Landis T, Burkhard PR. Restless arms. Lancet. 2008; **371**(9611): 530.
51. Balaskas EV. Uremic pruritus in CAPD patients. Perit Dial Int. 1997; **17**(5): 440-1.
52. Wikstrom B. Itchy skin--a clinical problem for haemodialysis patients. Nephrol Dial Transplant. 2007; **22 Suppl 5**: v3-7.
53. Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M. A questionnaire for the assessment of pruritus: validation in uremic patients. Acta Derm Venereol. 2001; **81**(2): 108-11.
54. Mettang T, Fritz P, Weber J, Machleidt C, Hubel E, Kuhlmann U. Uremic pruritus in patients on hemodialysis or continuous ambulatory peritoneal dialysis (CAPD). The role of plasma histamine and skin mast cells. Clin Nephrol. 1990; **34**(3): 136-41.
55. Lieberman JA. Update on the safety considerations in the management of insomnia with hypnotics: incorporating modified-release formulations into primary care. Prim Care Companion J Clin Psychiatry. 2007; **9**(1): 25-31.
56. Neutel CI, Patten SB. Sleep medication use in Canadian seniors. Can J Clin Pharmacol. 2009; **16**(3): e443-52.
57. Barbera J, Shapiro C. Benefit-risk assessment of zaleplon in the treatment of insomnia. Drug Saf. 2005; **28**(4): 301-18.
58. Claxton RN, Blackhall L, Weisbord SD, Holley JL. Undertreatment of symptoms in patients on maintenance hemodialysis. J Pain Symptom Manage. 2010; **39**(2): 211-8.

59. Pinto LR, Jr., Alves RC, Caixeta E, Fontenelle JA, Bacellar A, Poyares D, et al. New guidelines for diagnosis and treatment of insomnia. Arq Neuropsiquiatr. 2010; **68**(4): 666-75.
60. Morin CM, Colecchi C, Stone J, Sood R, Brink D. Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial. JAMA. 1999; **281**(11): 991-9.
61. Tentori F, Elder SJ, Thumma J, Pisoni RL, Bommer J, Fissell RB, et al. Physical exercise among participants in the Dialysis Outcomes and Practice Patterns Study (DOPPS): correlates and associated outcomes. Nephrol Dial Transplant. 2010; **25**(9): 3050-62.
62. Chen HY, Chiang CK, Wang HH, Hung KY, Lee YJ, Peng YS, et al. Cognitive-behavioral therapy for sleep disturbance in patients undergoing peritoneal dialysis: a pilot randomized controlled trial. Am J Kidney Dis. 2008; **52**(2): 314-23.
63. Morin C, Espie C. Insomnia - A clinical guide to assessment and treatment. New York: Springer; 2004.
64. Drummond SP, Smith MT, Orff HJ, Chengazi V, Perlis ML. Functional imaging of the sleeping brain: review of findings and implications for the study of insomnia. Sleep Med Rev. 2004; **8**(3): 227-42.
65. Caldwell JA, Prazinko B, Caldwell JL. Body posture affects electroencephalographic activity and psychomotor vigilance task performance in sleep-deprived subjects. Clin Neurophysiol. 2003; **114**(1): 23-31.
66. Thomas M, Sing H, Belenky G, Holcomb H, Mayberg H, Dannals R, et al. Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. J Sleep Res. 2000; **9**(4): 335-52.
67. Kutner NG, Zhang, R., Huang, Y., Bliwise, D. L. Patient-reported sleep difficulty and cognitive function during the first year of dialysis. Int Urol Nephrol. 2008; **40**(1): 203-10.
68. Stepanski E, Lamphere, J., Roehrs, T., Zorick, F., Roth, T. Experimental sleep fragmentation in normal subjects. Int J Neurosci. 1987; **33**(3-4): 207-14.
69. Adeseun GA, Rosas SE. The impact of obstructive sleep apnea on chronic kidney disease. Curr Hypertens Rep. 2010; **12**(5): 378-83.
70. Chiu YL, Chuang YF, Fang KC, Liu SK, Chen HY, Yang JY, et al. Higher systemic inflammation is associated with poorer sleep quality in stable haemodialysis patients. Nephrol Dial Transplant. 2009; **24**(1): 247-51.
71. Tack BB. Fatigue in rheumatoid arthritis. Conditions, strategies, and consequences. Arthritis Care Res. 1990; **3**(2): 65-70.
72. Piper BF, editor. Pathophysiological phenomena in nursing : human responses to illness. Philadelphia: Saunders; 1986.

73. Cantor F. Central and peripheral fatigue: exemplified by multiple sclerosis and myasthenia gravis. PM R. 2010; **2**(5): 399-405.
74. Jhamb M, Weisbord SD, Steel JL, Unruh M. Fatigue in patients receiving maintenance dialysis: a review of definitions, measures, and contributing factors. Am J Kidney Dis. 2008; **52**(2): 353-65.
75. Ream E, Richardson A. Fatigue: a concept analysis. Int J Nurs Stud. 1996; **33**(5): 519-29.
76. Hart L, Freel M, Milde F. Fatigue. Nurs Clin North Am. 1990; **28**(4): 967-76.
77. Jorgensen R. Chronic fatigue: an evolutionary concept analysis. J Adv Nurs. 2008; **63**(2): 199-207.
78. Brunier GM, Graydon J. The influence of physical activity on fatigue in patients with ESRD on hemodialysis. ANNA J. 1993; **20**(4): 457-61; discussion 62, 521.
79. Cella D, Lai JS, Chang CH, Peterman A, Slavin M. Fatigue in cancer patients compared with fatigue in the general United States population. Cancer. 2002; **94**(2): 528-38.
80. Hetta J, Almqvist M, Ågren H, Hambert G, Liljenberg G, Roos BE, editors. Prevalence of sleep disturbances and related symptoms in a middle-aged Swedish population. Stuttgart: Gustaf Fischer-Verlag; 1985.
81. Stein MB, Belik SL, Jacobi F, Sareen J. Impairment associated with sleep problems in the community: relationship to physical and mental health comorbidity. Psychosom Med. 2008; **70**(8): 913-9.
82. Kyle SD, Morgan K, Espie CA. Insomnia and health-related quality of life. Sleep Med Rev. 2010; **14**(1): 69-82.
83. Molnar MZ, Novak M, Mucsi I. Sleep disorders and quality of life in renal transplant recipients. Int Urol Nephrol. 2009; **41**(2): 373-82.
84. Bilgic A, Akman B, Sezer S, Ozisik L, Arat Z, Ozdemir FN, et al. Predictors for quality of life in continuous ambulatory peritoneal dialysis patients. Nephrology (Carlton). 2008; **13**(7): 587-92.
85. Soni RK, Weisbord SD, Unruh ML. Health-related quality of life outcomes in chronic kidney disease. Curr Opin Nephrol Hypertens. 2010; **19**(2): 153-9.
86. WHO. Basic documents - Constitution of the Worlds Health Organization. Geneva: WHO Press; 2009.
87. WHO. Frequently asked questions. [cited 2011-02-07]; Available from: http://www.who.int/suggestions/faq/en/
88. Unruh ML, Hess R. Assessment of health-related quality of life among patients with chronic kidney disease. Adv Chronic Kidney Dis. 2007; **14**(4): 345-52.
89. Polit D, Beck C. Nursing research: generating and assessing evidence for nursing practice. 8 ed. Philadelphia: Wolter Kluwer health/Lippincott Williams & Wilkins; 2008.

90. Edell-Gustafsson U, Carstensen J, Regestein Q, Swahn E, Svanborg E. Hyperarousal, depression and quality of life--validity and reliability of the Swedish version of the Hyperarousal Scale. Scand J Caring Sci. 2006; **20**(1): 58-67.
91. Ltd Neurotechnology Cambridge. Actiwatch Sleep Analysis 1.09. 2001.
92. Camtech. Actigraphy: Activity and Sleep Analysis. Cambridge Neurotechnology Ltd Information Bulletin No 4B. 2007.
93. Edell-Gustafsson U, Svanborg E, Swahn E. A gender perspective on sleeplessness behavior, effects of sleep loss, and coping resources in patients with stable coronary artery disease. Heart Lung. 2006; **35**(2): 75-89.
94. Yngman-Uhlin P, Edell-Gustafsson U. Self-reported subjective sleep quality and fatigue in patients with peritoneal dialysis treatment at home. Int J Nurs Pract. 2006; **12**(3): 143-52.
95. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. BMJ. 2002; **324**(7351): 1417.
96. Sullivan M, Karlsson J, Taft C. SF-36 Hälsoenkät: Svensk manual och tolkningsguide (Swedish Manual and Interpretation Guide). 2 ed. Gothenburg: Sahlgrenska University Hospital; 2002.
97. Walters AS, LeBrocq C, Dhar A, Hening W, Rosen R, Allen RP, et al. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. Sleep Med. 2003; **4**(2): 121-32.
98. Acebo C, LeBourgeois MK. Actigraphy. Respir Care Clin N Am. 2006; **12**(1): 23-30, viii.
99. Edell-Gustafsson UM, Hetta JE, Aren GB, Hamrin EK. Measurement of sleep and quality of life before and after coronary artery bypass grafting: a pilot study. Int J Nurs Pract. 1997; **3**(4): 239-46.
100. Morgan K, Closs J. Sleep management in nursing practice-an evidence-based guide. London: Churchill Livingston; 1999.
101. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage. 1997; **13**(2): 63-74.
102. Giorgi A. The descriptive Phenomenological method in psycology - A modified Husserlian Approch. 2 ed. Pittsburg: Duquesne University press; 2010.
103. Aukerman MM, Aukerman D, Bayard M, Tudiver F, Thorp L, Bailey B. Exercise and restless legs syndrome: a randomized controlled trial. J Am Board Fam Med. 2006; **19**(5): 487-93.
104. Al-Jahdali HH, Al-Qadhi WA, Khogeer HA, Al-Hejaili FF, Al-Ghamdi SM, Al Sayyari AA. Restless legs syndrome in patients on dialysis. Saudi J Kidney Dis Transpl. 2009; **20**(3): 378-85.

105. Yang A, Palmer AA, de Wit H. Genetics of caffeine consumption and responses to caffeine. Psychopharmacology (Berl). 2010; **211**(3): 245-57.
106. Gooley JJ. Treatment of circadian rhythm sleep disorders with light. Ann Acad Med Singapore. 2008; **37**(8): 669-76.
107. Morgan DL, Morgan RK. Single-Case Research Methods. Los Angeles: SAGE; 2009.
108. Siegel S, Castellan N. Nonparametric statistics for behavioural science. New York: McGraw -Hill; 1988.
109. Frost MH, Bonomi AE, Cappelleri JC, Schunemann HJ, Moynihan TJ, Aaronson NK. Applying quality-of-life data formally and systematically into clinical practice. Mayo Clin Proc. 2007; **82**(10): 1214-28.
110. Miles J, Shevlin M. Applying regression & correlation: a guide for students and researchers. London ; Thousand Oaks, Calif.: Sage Publications; 2001.
111. Field A, editor. Discovering statistics using SPSS (and sex and drugs and rock´n´roll). 3 ed. Dubai: Oriental Press; 2009.
112. Giorgi A. The descriptive phenomenology and psychological research. Pittsburgh: Duquesne University Press; 1985.
113. Giorgi A. The theory, practice, and evaluation of the phenomenological method as a qualitative research procedure. J Phenomenol Psyc. 1997; **28**(2): 235-60.
114. Stepanski EJ. The effect of sleep fragmentation on daytime function. Sleep. 2002; **25**(3): 268-76.
115. Aubert-Tulkens G, Culee C, Harmant-Van Rijckevorsel K, Rodenstein DO. Ambulatory evaluation of sleep disturbance and therapeutic effects in sleep apnea syndrome by wrist activity monitoring. Am Rev Respir Dis. 1987; **136**(4): 851-6.
116. Lichstein KL, Stone KC, Donaldson J, Nau SD, Soeffing JP, Murray D, et al. Actigraphy validation with insomnia. Sleep. 2006; **29**(2): 232-9.
117. Gislason T, Almqvist M. Somatic diseases and sleep complaints. An epidemiological study of 3,201 Swedish men. Acta Med Scand. 1987; **221**(5): 475-81.
118. Hetta JM, L. Bengtsson, H. Broman, J-E. . Polysomnographic versus questionairre data on difficulties falling asleep and total sleep time. Journal of Sleep Research. 1998; .
119. Sullivan M, Karlsson J, Ware JE, Jr. The Swedish SF-36 Health Survey I. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. Soc Sci Med. 1995; **41**(10): 1349-58.
120. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992; **30**(6): 473-83.

121. Abetz L, Arbuckle R, Allen RP, Garcia-Borreguero D, Hening W, Walters AS, et al. The reliability, validity and responsiveness of the International Restless Legs Syndrome Study Group rating scale and subscales in a clinical-trial setting. Sleep Med. 2006; **7**(4): 340-9.
122. Giorgi A, Giorgi B. The descriptive Phenomenological Psychological Method. In: Camic PM, Rhodes JE, Yardley L, editors. Qualitative research in psychology : expanding perspectives in methodology and design. 1st ed. Washington, DC: American Psychological Association; 2003. p. xvi, 315 p.
123. WMA. World medical association declaration of helsinki. Etical principles for medical research involving human subjects. 2008 [cited; Available from: http://www.wma.net/en/30publications/10policies/b3/index.html
124. Yngman-Uhlin P, Friedrichsen M, Gustavsson M, Fernstrom A, Edell-Gustafsson U. Circling around in tiredness: perspectives of patients on peritoneal dialysis. Nephrol Nurs J. 2010; **37**(4): 407-13.
125. Heiwe S CN, Abrandt Dahlgren M. Living with renal failure: patients´ experiences of their physical and functional capacity. Physiotherapy research international. 2003; **8**(4): 167-77.
126. Hui DS, Wong TY, Ko FW, Li TS, Choy DK, Wong KK, et al. Prevalence of sleep disturbances in chinese patients with end-stage renal failure on continuous ambulatory peritoneal dialysis. Am J Kidney Dis. 2000; **36**(4): 783-8.
127. Stepanski E, Faber M, Zorick F, Basner R, Roth T. Sleep disorders in patients on continuous ambulatory peritoneal dialysis. J Am Soc Nephrol. 1995; **6**(2): 192-7.
128. Morin CM, LeBlanc M, Daley M, Gregoire JP, Merette C. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Med. 2006; **7**(2): 123-30.
129. Doghramji K. The epidemiology and diagnosis of insomnia. Am J Manag Care. 2006; **12**(8 Suppl): S214-20.
130. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurence of sleepdisordered breathing among middle-age adults. The New England Journal of medicine. 1993; **328**(17): 1230-5.
131. American Sleep Disorders Association Atlas Task force. EEG arousals: scoring rules and examples. SLEEP. 1992; **15**: 173-84.
132. Tranaeus A, Yao Q. Immune dysfunction in dialysis patients--prevention and treatment strategies. Perit Dial Int. 2008; **28 Suppl 3**: S161-6.
133. Mullington J, Haack M, Toth M, Serrado J, Meier-Ewert H. Cardiovascular, inflammatory, and metabolic consequenses of sleep deprevation. Prog Card Dis. 2009; **51**(4): 294-302.
134. Lugon JR. Uremic pruritus: a review. Hemodial Int. 2005; **9**(2): 180-8.

135. Pisoni RL, Wikstrom B, Elder SJ, Akizawa T, Asano Y, Keen ML, et al. Pruritus in haemodialysis patients: International results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant. 2006; **21**(12): 3495-505.
136. Lui SL, Ng F, Lo WK. Factors associated with sleep disorders in Chinese patients on continuous ambulatory peritoneal dialysis. Perit Dial Int. 2002; **22**(6): 677-82.
137. Enomoto M, Inoue Y, Namba K, Munezawa T, Matsuura M. Clinical characteristics of restless legs syndrome in end-stage renal failure and idiopathic RLS patients. Mov Disord. 2008; **23**(6): 811-6; quiz 926.
138. Allen RP. Improving RLS diagnosis and severity assessment: polysomnography, actigraphy and RLS-sleep log. Sleep Med. 2007; **8 Suppl 2**: S13-8.
139. Kumagai TI, Y. Kawarazaki, W. Shimizu, H Kaname, S. Fujita T. Effects of nocturnal oxygen theraphy on sleep apnea syndrome in peritoneal dialysis patients. Clin Nephrol. 2008; **70**(4): 332-9.
140. Mavanur M, Sanders M, Unruh M. Sleep disordered breathing in patients with chronic kidney disease. Indian J Med Res. 2010; **131**: 277-84.
141. Hanly PJ, Pierratos A. Improvement of sleep apnea in patients with chronic renal failure who undergo nocturnal hemodialysis. N Engl J Med. 2001; **344**(2): 102-7.
142. Kuniyoshi FH, Pusalavidyasagar S, Singh P, Somers VK. Cardiovascular consequences of obstructive sleep apnoea. Indian J Med Res. 2010; **131**: 196-205.
143. Loewen A, Siemens A, Hanly P. Sleep disruption in patients with sleep apnea and end-stage renal disease. J Clin Sleep Med. 2009; **5**(4): 324-9.
144. Iliescu EA, Yeates KE, Holland DC. Quality of sleep in patients with chronic kidney disease. Nephrol Dial Transplant. 2004; **19**(1): 95-9.
145. Ossareh S, Roozbeh, J. Krishnan, M. Bargman, JM. Oreopoulos, DG. Fatigue in peritoneal dialysis patients. Int Urol and Nephrol. 2003; **35**: 535-41.
146. Jhamb M, Argyropoulos C, Steel JL, Plantinga L, Wu AW, Fink NE, et al. Correlates and outcomes of fatigue among incident dialysis patients. Clin J Am Soc Nephrol. 2009; **4**(11): 1779-86.
147. Lee B, Lin, C-C., Chaboyer, W., Chiang, C-L., Hung, C-C. The fatigue experiences of haemodialysis patients in Taiwan. J Clin Nurs 2003; (16): 407-13.
148. Goodchild CE, Treharne GJ, Booth DA, Bowman SJ. Daytime patterning of fatigue and its associations with the previous night's discomfort and poor sleep among women with primary Sjogren's syndrome or rheumatoid arthritis. Musculoskelet Care. 2010; **8**: 107-17.

149. Hossain JL, Ahmad P, Reinish LW, Kayumov L, Hossain NK, Shapiro CM. Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders? J Sleep Res. 2005; **14**(3): 245-53.
150. Singareddy R, Bixler EO, Vgontzas AN. Fatigue or daytime sleepiness? J Clin Sleep Med. 2010; **6**(4): 405.
151. Young TB. Epidemiology of daytime sleepiness: definitions, symptomatology, and prevalence. J Clin Psychiatry. 2004; **65 Suppl 16**: 12-6.
152. Zucker I, Yosipovitch G, David M, Gafter U, Boner G. Prevalence and characterization of uremic pruritus in patients undergoing hemodialysis: uremic pruritus is still a major problem for patients with end-stage renal disease. J Am Acad Dermatol. 2003; **49**(5): 842-6.
153. Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep. 2003; **26**(2): 117-26.
154. Kutner NG, Zhang R, Huang Y, Bliwise DL. Patient-reported sleep difficulty and cognitive function during the first year of dialysis. Int Urol Nephrol. 2008; **40**(1): 203-10.
155. Milner CE, Cote KA. Benefits of napping in healthy adults: impact of nap length, time of day, age, and experience with napping. J Sleep Res. 2009; **18**(2): 272-81.
156. WHO. The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research Geneva: WHO; 1993.
157. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. J Am Geriatr Soc. 2005; **53**(1): 48-53.
158. Knutson KL. Impact of sleep and sleep loss on glucose homeostasis and appetite regulation. Sleep Med Clin. 2007; **2**(2): 187-97.
159. Redwine L, Hauger RL, Gillin JC, Irwin M. Effects of sleep and sleep deprivation on interleukin-6, growth hormone, cortisol, and melatonin levels in humans. J Clin Endocrinol Metab. 2000; **85**(10): 3597-603.
160. Ekholm O, Hesse U, Davidsen M, Kjoller M. The study design and characteristics of the Danish national health interview surveys. Scand J Public Health. 2009; **37**(7): 758-65.
161. Wang SY, Chang HJ, Lin CC. Sleep disturbances among patients with non-small cell lung cancer in Taiwan: congruence between sleep log and actigraphy. Cancer Nurs. 2010; **33**(1): E11-7.
162. Knutson KL, Rathouz PJ, Yan LL, Liu K, Lauderdale DS. Intra-individual daily and yearly variability in actigraphically recorded sleep measures: the CARDIA study. Sleep. 2007; **30**(6): 793-6.

163. Wolfe F, Michaud K. The Hawthorne effect, sponsored trials, and the overestimation of treatment effectiveness. J Rheumatol. 2010; **37**(11): 2216-20.
164. Riegel B, Carlson B, Kopp Z, LePetri B, Glaser D, Unger A. Effect of a standardized nurse case-management telephone intervention on resource use in patients with chronic heart failure. Arch Intern Med. 2002; **162**(6): 705-12.
165. Wong FK, Chow SK, Chan TM. Evaluation of a nurse-led disease management programme for chronic kidney disease: a randomized controlled trial. Int J Nurs Stud. 2010; **47**(3): 268-78.
166. Brooten D, Youngblut JM. Nurse dose as a concept. J Nurs Scholarsh. 2006; **38**(1): 94-9.
167. Cella D, Zagari MJ, Vandoros C, Gagnon DD, Hurtz HJ, Nortier JW. Epoetin alfa treatment results in clinically significant improvements in quality of life in anemic cancer patients when referenced to the general population. J Clin Oncol. 2003; **21**(2): 366-73.
168. Norman GR, Sloan JA, Wyrwich KW. The truly remarkable universality of half a standard deviation: confirmation through another look. Expert Rev Pharmacoecon Outcomes Res. 2004; **4**(5): 581-5.
169. Sloan JA, Cella D, Hays RD. Clinical significance of patient-reported questionnaire data: another step toward consensus. J Clin Epidemiol. 2005; **58**(12): 1217-9.
170. Barlow DH, Hersen M. Single case experimental designs : strategies for studying behavior change. 2nd ed. New York: Pergamon Press; 1984.
171. WHO. WHO definition of palliative care. 2011 [cited 2011-02-05]; Available from: http://www.who.int/cancer/palliative/definition/en/
172. Al-Jahdali HH, Khogeer HA, Al-Qadhi WA, Baharoon S, Tamim H, Al-Hejaili FF, et al. Insomnia in chronic renal patients on dialysis in Saudi Arabia. J Circadian Rhythms. 2010; **8**: 7.
173. Novak M, Shapiro CM, Mendelssohn D, Mucsi I. Diagnosis and management of insomnia in dialysis patients. Semin Dial. 2006; **19**(1): 25-31.
174. Riegel B, Dickson VV, Cameron J, Johnson JC, Bunker S, Page K, et al. Symptom recognition in elders with heart failure. J Nurs Scholarsh. 2010; **42**(1): 92-100.
175. Puntillo K, Neighbor M, O´Neil N. Emergency Department Nurses' and Patients' Estimates of patient Pain: How Close Are They? Abstract presented at ENA Annual meeting, Washington DC. 1999.
176. Dodd M, Janson S, Facione N, Faucett J, Froelicher ES, Humphreys J, et al. Advancing the science of symptom management. J Adv Nurs. 2001; **33**(5): 668-76.
177. Bloom HG, Ahmed I, Alessi CA, Ancoli-Israel S, Buysse DJ, Kryger MH, et al. Evidence-based recommendations for the assessment and

management of sleep disorders in older persons. J Am Geriatr Soc. 2009; **57**(5): 761-89.
178. Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. Clin J Am Soc Nephrol. 2009; **4**(6): 1057-64.
179. Morgan K, Closs J, editors. Sleep management in nursing practice-an evidence-based guide. London: Churcill Livingston; 1999.