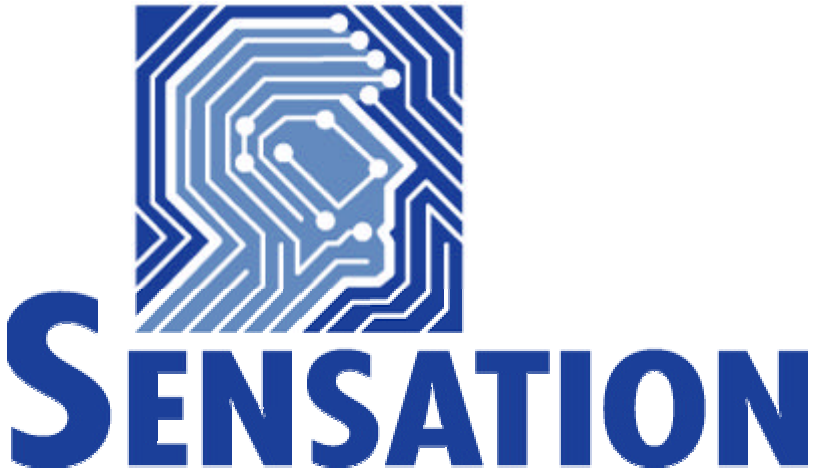
INFORMATION SOCIETY TECHNOLOGIES (IST) PROGRAMME



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List of requirements and proposed standards

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Abbreviations

AHI:	Apnea-Hypopnea Index
AASM:	American Academy of Sleep Medicine
ACCP:	American College of Chest Physicians
ASDA:	American Sleep Disorders Association
ATS:	American Thoracic Society
AUTH:	Aristotle University of Thessaloniki
CPAP:	Continuous Positive Airway Pressure
D:	Deliverable
DIMS:	Disorders of Initiating and Maintaining Sleep
DOES:	Disorders of Excessive Somnolence
EDS:	Excessive Daytime Sleepiness
EEG:	Electroencephalogram
EMG:	Electromyogram
EOG:	Electrooculogram
ESS:	Epworth Sleepiness Scale
HoSD:	Home Polysomnography
HRV:	Heart Rate Variability
ICD:	International Code of Diseases
ICSD:	International Classification of Sleep Disorders
KSS:	Karolinska Sleepiness Scale
MSLT:	Multiple Sleep Latency Tests
MWT:	Maintenance of Wakefulness Test
OSA:	Obstructive Sleep Apnea
OSAS:	Obstructive Sleep Apnea Syndrome
OSAHS:	Obstructive Sleep Apnea/Hypopnea Syndrome
NCPAP:	Nasal continuous positive airway pressure
PLMD:	Periodic Limb Movement Disorder
PAT:	Peripheral Arterial Tone
PDS:	Portable Diagnostic System
PSG:	Polysomnography
PVT:	Psychomotor Vigilance Test
QOL:	Quality of Life
RIP:	Respiratory Inductance Plethysmography
RLS:	Restless Legs Syndrome
SaO_2:	Oxygen Saturation
SAS:	Sleep Apnea Syndrome
SP:	Subprojects
WP:	Work Package
WHO:	World Health Organization

Executive Summary

SP3 is the SENSATION subproject that will define, in which medical applications we will apply and evaluate the developed algorithms and sensors from SP1 and SP2 respectively. In SP3 we will also integrate the developed algorithms and sensors into a complete distance monitoring system that will enable the "anytime, anywhere" monitoring of patients with sleep disorders. A "telemedicine system" will be developed where clinical, technical, organizational and practical issues need to be assessed. This system will be tested and evaluated through medical pilots.

WP3.1 will provide the user requirements of this distance monitoring system. The first task in WP3.1 has been to assess the current status of distance monitoring in sleep disorder applications and to propose preliminary requirements for the system that will be developed. The current document, D3.1.1 is the outcome of this work.

The main activity during the first five project months has been the literature search for ambulatory monitoring (not in lab environment) for patients with sleep disorders. Four interviews with sleep disorder clinical specialists were also performed in order to receive experts' feedback on the current management procedures of sleep disorders as well as their expectations from SENSATION. Finally, one focus group meeting took place in April 2004 in order to provide a preliminary set of requirements in the form of user scenarios. Conclusions of this work are summarized below.

Medical applications will focus both on sleep and sleepiness/drowsiness monitoring. Clinicians agree that SENSATION should be applied in the diagnosis of patients with insomnia, and/or hypersomnia complaints.

Distance monitoring for patients with sleep disorders is currently applied in the in-home diagnosis and (less often) treatment follow-up of Obstructive Sleep Apnea. Several portable devices exist in the market; however, reviews and evaluation studies have shown that home studies using portable devices are not reliable. As a result, the most recent official guidelines in US do not recommend the use of such devices. In Europe the use of portable devices varies, depending on the re-imbursement procedures that exist in each country. A system like SENSATION will be able to be used in a clinical setting only if it is thoroughly tested and validated in an unattended setting and it has to be compared against standard in lab procedures (e.g. PSG for the case of Obstructive Sleep Apnea). Therefore, particular emphasis should be paid in the setup and implementation of medical trials in SP3. SENSATION

should also contribute in the generation of common guidelines in Europe, for the use of such equipment.

A major requirement from the clinicians has been the need for at least one EEG measurement by using reliable, dry, and stable EEG sensors through a portable device for studying both sleep disorders and/or sleepiness/drowsiness. At least one EEG for sleep, one EOG, one ECG and one EMG raw data signal should be available in the developed system. More sensitive oxygen saturation and body temperature sensors have been required to be used in sleep studies. An automated artifact rejection algorithm has also been required. More advanced algorithms for sleep staging evaluation based on Peripheral Arterial Tone signal should be developed. Sleepiness monitoring requires two EEGs and one EOG. The development of a camera-based micro sensor for EOG and motility parameters for studying drowsiness should also be useful. The developed sensors have to be integrated in a telemedicine system that will allow long term follow up of patients with sleep disorders anytime-anywhere.

In the following six months, detailed scenarios for remote monitoring of sleep and sleepiness have to be generated. These will lead to the detailed list of user requirements for the SENSATION System(s).

1. Introduction

SP3 is the subproject that will define, in which medical applications we will apply and evaluate the developed algorithms and sensors from SP1 and SP2 respectively. In SP3 we will also integrate the developed algorithms and sensors into a complete distance monitoring system that will enable the "anytime, anywhere" monitoring of patients with sleep disorders. A "telemedicine system" will be developed where clinical, technical, organizational and practical issues need to be assessed. This system will be tested and evaluated through medical pilots.

WP3.1 will provide the user requirements of this distance monitoring system. Specifically, the objectives of this work package are:

- To trace the current clinical trends as well as likely application scenarios for the techniques, tools, and sensors developed in SP1 and SP2.
- To understand the requirements for the clinical monitoring of sleep/wakefulness, vigilance attention and stress identification.
- To analyse the requirements in terms of actual difficulties as encountered by patients and clinicians for the applications.

According to the technical annex, the tasks that have to be performed in WP3.1, in chronological order, are:

- Month 6: Performance of literature review.
- Month 12: User requirements and scenarios.
- Month 15: Transcription of the focus group discussions.
- Month 17: Workshop on selection of clinical application priorities/scenarios.

The first task in WP3.1 has been to perform literature review in order to assess the current status of distance monitoring in sleep disorder applications. Definition of user requirements and scenarios are planned for month 12. Therefore the current document focuses on the literature review for ambulatory monitoring systems for in-home assessment on sleep disorders as well as for existing guidelines for the use of such systems. Since the first interviews and focus group meeting have already been conducted, initial user requirements have also been included. Starting from this list, as well as from requirements collected from other WPs, more interviews will be conducted in the following six months in order to define in detail user requirements and pilot application protocols that will be presented in D3.1.2, in project month 12.

The remainder of this document is structured as follows: Section 2 presents the activities that were performed during the first 5 project months. Section 3 gives an overview and classification of sleep disorders, while Section 4 describes in detail the current status of distance monitoring for patients with sleep disorders. In Section 5, proposed medical applications for SENSATION project are defined. Finally, in Section 6 conclusions are summarized and initial requirements are presented.

2. Methodology

In order to report on the current clinical applications that are related to ambulatory monitoring (not in a lab environment) for patients with sleep disorders, three main activities, namely interviews with physicians, literature review and a focus group, took place during the first five project months. They are briefly described below.

2.1. Activity 3.1.1: Literature Search

Literature search was performed by AUTH in order to find what ambulatory monitoring systems exist for in-home assessment on sleep disorders as well as existing guidelines for the use of such systems. Literature search includes issues such as the current status of ambulatory monitoring systems, the outcome of evaluation studies and trials, and the expectations of the clinicians for the future.

In the first phase of literature search, Medline was searched extensively from 1990 until Feb 29, 2004. Search was based on the following topics: “sleep disorders ambulatory monitoring” and “portable sleep”. Then all available abstracts were printed and reviewed. Studies reported in English were accepted.

In order to be included in the review, studies had to report:

- Description/review of an in-home ambulatory technique,
- or intervention that supported in-home diagnosis or treatment follow-up on any sleep disorder,
- or guidelines for portable device use,
- or procedures and scenarios of use of EEG, EMG, EOG and heart rate in in-home sleep disorders diagnosis and treatment

As a result, 60 articles were indexed and stored (references 57-116). Some of these articles were also recommended during the interviews. The findings of this search are discussed in detail in Section 4.

2.2. Activity 3.1.2: Interviews with physicians

Interviews with domain experts or less experienced users is a commonplace method for obtaining in depth data about a particular user role or set of tasks. In the context of WP3.1 approximately 30 interviews are expected to be carried out by project month 16. An initial phase of 4 interviews ran in parallel with literature review in order to obtain an overview of the management of sleep disorders and receive guidelines and assistance in the literature review process. However, most interviews have been planned for the second part of WP3.1 (Project Month 7 to Project Month 12) where in depth data on user home care needs, security requirements and educational needs will be provided by domain experts.

Four interviews with physicians from three European Countries took place in February 2004. The interviewed physicians are all specialists in sleep disorders, each one however, with different medical specialization: one physiologist (Germany), one psychiatrist (France), one neurologist (Greece) and one pneumonologist (Greece).

Three phone interviews and one face-to-face interview were performed. All interviews were semi-structured. The outline of the questions was e-mailed to the participants prior to the interview, so that they could be prepared (APPENDIX I). Synopsis of each interview separately is included in APPENDIX II, while feedback from all interviews is presented in Sections 3, 4, 5 and 6.

The main topics discussed in the interviews were:

- Overview of the management of sleep disorders in their countries.
- Current status of ambulatory monitoring of sleep disorders, comparison of in-lab and in-home assessment.
- Report on devices they have used for in-home assessment
- Suggestions on literature search.
- Suggestions on the clinical applications that could be appropriate for SENSATION.

Material from the interviews is presented in Sections 3, 4, 5 and 6.

2.3. Activity 3.1.3: Focus Group Meeting

One focus group (APPENDIX IV) was organized in Project Month 4 in Barcelona, aiming to describe two realistic scenarios for distance monitoring of patients with sleep disorders. As this has been the first focus group meeting, one

general scenario was proposed for sleep monitoring and is presented below. A preliminary set of requirements has resulted from this focus group meeting. All requirements are presented in Tables 11, 12, 13, 14, 15, and 16. The detailed user requirements and scenarios, as stated in the Technical Annex, will be specified between project month 6 and 12, and will be reported in D3.1.2.

3. Overview and Classification of sleep disorders

3.1. Sleep and Excessive Daytime Sleepiness

Sleep is a reversible behavioral state of perceptual disengagement from unresponsiveness to the environment. Sleep is a complex amalgam of physiological and behavioral processes. Sleep is usually, accompanied by postural recumbence, quiescence, closed eyes, and all the other indicators associates with sleeping. Other behaviors may include sleepwalking, sleep talking, tooth grinding, and other physical activities. Anomalies involving sleep processes also include intrusions of the sleep processes-sleep itself, dream imagery, or muscle weakness- into wakefulness.

Within sleep, two separate states have been defined on the basis of a constellation of physiological parameters. NREM – non rapid eye movement and REM –rapid eye movement, exist in virtually all mammals and are as distinct from one another as each is from wakefulness [1].

Scientific and clinical attention to sleepiness arose from the recognition of excessive daytime sleepiness (EDS) as a symptom associated with serious life-threatening medical conditions. Excessive daytime sleepiness is a common complaint in general medical practice. Certainly the most frequent cause is the use of any one of the huge variety of medications that are not prescribed for their sedative effect. Abuse of alcohol and illicit drugs should also be included. Infectious diseases (i.e. mononucleosis), neurological conditions (i.e. multiple sclerosis, dementia), metabolic derangements (hypothyroidism, Addison disease, hypercapnia), sleep apnea are associated with severe fatigue produce daytime sleepiness and desire to nap.

In the late 1960s, this symptom attributed to lifestyle excess, viewed as a sign of laziness and malingering, or seen as assign of narcolepsy. Patients with daytime sleepiness typically complain of drowsiness that interferes with daytime activities, unavoidable napping, or both. Drowsiness and naps either may be limited to sedentary situations in which falling asleep in socially acceptable, such as watching TV or reading at home, or may occur at work, while driving, in conversation, sitting on the toilet or during sexual intercourse.

3.2. Sleep-related Symptoms

Loud snoring, gasping, snorting and episodes of apnea suggest the diagnosis of sleep apnea-hypopnea syndrome. The relationship of snoring to body position should be determined; snoring may occur in all positions or only in the supine. A history of episodic muscle weakness with buckling of the knees, laxity of the neck or jaw muscles, or complete loss of muscle tone associated with laughter or other emotions suggest cataplexy and a diagnosis of narcolepsy. Episodes of partial or total paralysis (sleep paralysis) and dream like auditory, visual, or tactile hallucinations occurring at sleep onset or on awakening also suggest narcolepsy. Questions assessing mood are needed to identify patients with sleep disorder associated with mood disorders. Short nocturnal sleep time, longer sleep on weekends or days off, and fewer symptoms during vacations when the period is longer suggest the insufficient sleep syndrome.

Circadian rhythm sleep disorders should be considered in patients with complaints of nocturnal insomnia and daytime sleepiness. Patients with delayed sleep-phase syndrome frequently complain of difficulty waking up, morning sleepiness and sluggishness, and difficulty falling asleep at night. Symptoms are worse on days when the patient must awaken by a set time. Patients with advanced sleep phase syndrome may complain of evening sleepiness and early morning awakening. The patient's occupation and social schedule may suggest diagnoses of shift work sleep disorder or jet lag syndrome.

Variations in prevalence daytime sleepiness depend on the population sampled and the questions asked. In a survey representative of the Finnish population, 11% of women and 7% of reported daytime sleepiness almost every day [2]. In another one, representative of a large geographical area in Sweden, 12% of respondents thought their sleep was insufficient [3].

3.3. Common Sleep Disorders

Insomnia is the primary problem in some patients compared to a symptom of other disorders. The International Classification of Sleep Disorders (ICSD) [4] defines insomnia as difficulty in initiating and / or maintaining sleep''. A recent working group of the National Center for Sleep Disorders Research (USA) stated,'' Insomnia

is an experience of inadequate or poor sleep characterized by one of the following: difficulty falling asleep, difficulty maintaining sleep, waking up too early in the morning, non refreshing sleep''. Insomnia also involves daytime consequences, such as tiredness, lack of energy, difficulty concentrating, and irritability [5]. The insomnia criteria [6] were one or more of the following symptoms nearly every night: 1.at least 2 hours to fall asleep, 2.lying awake at least 1 hour, 3.waking at least at least 2 hours early. Ford and Kamerow [7] used a more stringent definition to estimate insomnia prevalence in a 6-month time period for those 18 years and older in community sample. They required trouble falling asleep, staying asleep, or waking up too early, that: (1) lasted for at least 2 weeks, (2) interfered with their life a lot, (3) was not always the result of medical illness, medication, or drug/alcohol use, (4) about which professional was informed or medications were taken. With this definition 10.2% of the sample were said to have insomnia and 3% continued to have insomnia 1 year later.

An estimated prevalence for chronic insomnia is about 10%. When considering insomnia of any duration and severity, between 30% and 50% of the general population appears to be affected. Women are about 1.3 times more likely to report insomnia and elderly have approximately 1.3 times higher prevalence rates. Some types of insomnia are not caused by problems such as anxiety, depression, pain, allergy, or restless leg syndrome. For these types of insomnia, the term primary is used in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition DSM-IV [9]. The ICSD [4] does not recognize a category of primary insomnia, but discusses three freestanding subgroups: psychophysiological insomnia, sleep state misperception, and idiopathic insomnia.

Patients with primary insomnia are usually hyperaroused. They commonly show an increased metabolic rate [10], increased body temperature, and increased fast activity on the electroencephalogram (EEG) (greater than 20 Hz), both awake and long into sleep [11, 12]. Recent research suggests that insomnia may be much more like caffeine intoxication than like sleep deprivation [13]. Indeed, Bonnet and Arand [10] even suggested that insomnia may be the organism's attempt at curing excessive hyperarousal by slowing it down through sleep deprivation.

The vast majority of insomniac patients underestimate the amount of time they actually sleep. This may be related to the finding that sufferers have more fast EEG

frequencies during sleep, which may facilitate cognitive processes and interfere with the normal establish of mesograde amnesia [14].

In some patients the above-discussed underestimation may be extreme. Such patients are said to suffer from sleep state misperception syndrome. Patients with sleep-state misperception are very similar to those patients who have 'bona fide' insomnia: they have similar difficulties falling asleep, they take naps during the day and they show considerable hyperarousal [15, 16]. They respond to the same treatments (pharmacological, behavioral).

Treatment strategies are grouped in the following three domains: (1) sleep hygiene, (2) behavioral treatment, (3) hypnotics. Hypnotics are indicated in psychophysiological insomnia for poor nights, to be used no more than once or twice per week. They are prescribed to break the vicious cycle of patients needing sleep so desperately that they seek it too much and they are hyperaroused. It would be unwise to prescribe hypnotics during the time that behavioral treatment is learned [17].

Idiopathic insomnia is a lifelong inability to obtain adequate sleep. It may be that these patients are simply hyperaroused on an organic basis [10]. Insomnia is due to an abnormality in the neurological control of sleep-wake system. It involves many areas of the reticular activating, as well as wide-ranging sleep-inducing circuits in the areas of the solitary tract nuclei, the raphe nuclei, and the medial forebrain area. Idiopathic insomnia may involve the extreme end tending toward arousal, or possibly even a yet-to-be identified neuronatomical, neurophysiological, or neurochemical weakness in the sleep system or excessive strength in the arousal system [18]. People with idiopathic insomnia often show atypical reactions to medications, such as hypersensitivity or insensitivity. Some patients have responded to tricyclic antidepressants, some others to neuroleptic drugs. In addition supportive psychological treatment is often necessary.

Obstructive sleep apnea syndrome (OSAS) is the most common organic disorder causing excessive daytime sleepiness in patients referred to sleep centers. The disorder is called apnea-hypopnea syndrome (OSAHS) [19]. It is characterized by episodes of complete or partial pharyngeal obstruction during sleep.

Apnea is defined as the cessation of air flow for a minimum of 10 sec. Apneas are usually associated with sleep fragmentation and 2% to 4% drop in oxygen

saturation. Hypopnea is defined as a reduction 30%-50% in airflow for a minimum of 10 sec.

According to various cross-sectional studies, the lowest rates for the prevalence of OSAS among adult men are 1% to 4%. There is an age relationship, so the prevalence of OSAS among men 40 to 59 years old may be greater than 4% to 8%. OSAS is less common is younger and old age groups.

Obstructive sleep apnea events are also found as part of the 'heavy snorer's disease' as defined by Lugaresi et al [20]. Heavy snoring (i.e. partial upper airway obstruction) even without apneas may influence pulmonary arterial pressure, and it may cause daytime sleepiness and have some health consequences. The presence of sleep apnea is a potential determinant of risk in the same way as high blood pressure. According to epidemiological studies about 10%-15% of ''occasional or never snorers may have occasional obstructive sleep apneas [21]. Measurement of apneas necessitates a sleep recording. The basis of diagnosis is proper history taking (also from cohabiting persons) and clinical examination.

Patients with kyphoscoliosis and hereditary myopathy may have breathing problems in sleep. Obesity, male gender, family history, alcohol ingestion, tobacco use of sedatives, sleep deprivation and supine position are risk factors for OSAHS syndrome. Hypertension, cardiovascular diseases, metabolic diseases, hypothyroidism, gastro esophageal reflux, dementia, brain infarcts, Parkinson disease, Marfan's disease, Down syndrome are considered as predisposing factors for OSAHS syndrome.

Sleep apnea should be properly quantified, not only by an apnea index (AHI) but also by the length of the apnea events, extend and number of desaturations, limitation of air flow, cardiac manifestations associated with the breathing events. An AI of five events per hour of sleep is often used as a criterion of OSAS [22, 23]. An overnight monitoring must demonstrate five or more apneas plus hypopnea plus respiratory effort-related arousals per hour of sleep [19].

The upper airway resistance syndrome (UARS) is a sleep related breathing disorder being under current scientific debates described by an increased breathing effort during periods of increased upper airway resistance but without hypopnea or apnea events. These patients also present daytime sleepiness.

The most common symptoms and observations made by a bed partner are snoring, excessive daytime sleepiness, nocturnal snorting and gasping and witnessed

apneas. Nocturnal symptoms (snoring, witnessed apneas, choking, dyspnoea, restlessness, nocturia, diaphoresis, reflux, drooling) tend to be more specific for OSAHS than daytime symptoms (sleepiness, fatigue, morning headaches, poor concentration, decreased libido or impotence, decreased attention, depression, decreased dexterity, personality changes) are usually a result of abnormal sleep regardless of the cause.

There are clinical features associated with OSAHS such as obesity (BMI>28kg/m), neck circumference >40 cm, enlarged nasal turbinates, deviated nasal septum, narrow mandible, narrow maxilla, dental overjet and retrognathia, cross-bite and dental malocclusion, high and narrow hard palate, elongated and low-lying uvula, prominent tonsillar pillars, enlarged tonsils and adenoids, macroglossia.

OSAS is characterized by repetitive apneas during sleep. Then main symptoms of the disease are loud and irregular snoring, restless sleep, and daytime sleepiness.

In Israel, Lavie [24] estimated in a cross-sectional study that the prevalence among male industrial workers is at least 1%. Peter et al. reported a much higher prevalence of OSAS in Germany. Another epidemiological study was conducted in Bologna in Italy [25] the prevalence estimations of OSAS were 3.4% and 5%. In Scandinavian countries Gislason et al (26) reported a prevalence rate of 1.3% in a Swedish 30- to 69-year-old population. The prevalence of OSAS among 40- to50-year-old Finnish men is 0.4% and 1.4% [21].

OSAHS may be a lethal disease if not treated. There are several studies showing an increased risk of cardiovascular complications and death in patients with at least moderate (AHI more than 20 /h) or severe (AHI more than 40 /h) OSAHS.

Nasal continuous positive airway pressure (NCPAP) is the effective treatment of OSAS. Among obese patients, weight loss can reduce the number of apnea events as long as the subjects do not gain back the weight. There is still a lack of well –done prospective epidemiological studies proving the long-term effect of n-CPAP in mild OSAS, in simple snoring, and in upper airway resistance syndrome. Different surgical methods have been developed to treat snoring and OSAS. Uvulopalatopharyngoplasty and different laser techniques have been used to treat snoring and sleep apnea, but there are only a few studies, which could show effective treatment based on acceptable epidemiological methodology.

Janson et al. [31] studied the long term effects of uvulopalatopharyngoplasty in 34 patients with OSAS. Response to treatment was defined as 50% or greater

reduction in AHI of 10 /h or less. Sixty-four percent were responders at 6 months and 48% were responders at 4 to 8 years after surgery. None of the seven patients with an initial AHI of more than 40 /h were responders.

Parasomnias have been identified as a major category of sleep disorders including sleep talking, sleep bruxism, sleepwalking, sleep terrors, sleep enuresis, nightmares. They represent a group of physiological and behavioral phenomena that occur predominantly during sleep. Parasomnias are disorders of arousal, partial arousal, and sleep stage transition.

Narcolepsy is important because it is a key sleep disorder where the disturbed sleep itself is the primary finding. The term narcolepsy refers to a syndrome of unknown origin that is characterized by abnormal sleep tendencies, including excessive daytime sleepiness and often disturbed nocturnal sleep and pathological manifestations of REM sleep. The REM sleep abnormalities include sleep onset REM periods and the dissociated REM sleep inhibitory processes, cataplexy and sleep paralysis and hypnagogic hallucinations are the major symptoms of the disease [32]. The definition strongly emphasizes that the syndrome involves a dysfunction of REM sleep. It ignores, however, the notion that genetic factors are frequently involved. Moreover, although most cases of narcolepsy are idiopathic, secondary causes of narcolepsy have been described [33].

Narcolepsy is a rare disorder. Its prevalence is about 0,05% [34, 35] (other prevalence studies in Great Britain, France, Czech Republic and USA). The highest prevalence comes from Japan. Honda et al. interviewed symptomatic Japanese school-aged children selected by questionnaire and found ‘’suspect of narcolepsy’’ in 160 per 100,000. The lowest frequency, 0,23 per 100,000 population, is based on seven narcoleptics among 1800 polygraphically examined patients with EDS. In Israel, only a few narcoleptic patients were identified when compared to the large population of subjects recruited into sleep clinics. This has led to the suggestion that the prevalence of narcolepsy could be as low as 0,002% in this population. Males are affected more often than females. The age of onset varies from childhood to the fifth decade, with a peak in the second decade. Special circumstances, such as an abrupt change in sleep-wake schedule or a severe psychological stress, precede the occurrence of the first symptom in half of the cases.

The development of human narcolepsy involves environmental factors acting on a specific genetic background [36, 37, 38]. More than 85% of all narcoleptics with

definite cataplexy share a specific human leukocyte antigen (HLA) allele on chromosome 6, HLA DQB1*0602, most often in combination with HLADR15 [39]. This allele is also present in 12%-38% of the general population. Some patients with narcolepsy do not have the genetic marker [41]. A second gene involved in narcolepsy, the orexin (or hypocretin) gene, has been located. This gene is involved in the control of the hypocretin receptor. Hypocretin could not be detected in the cerebrospinal fluid of most people with narcolepsy, suggesting the role of abnormal hypocretin transmission.

The ICSD diagnostic criteria [4] include the classic tetrad for narcolepsy of excessive daytime sleepiness, cataplexy, sleep paralysis, and hypnagogic hallucinations. Automatic behaviors and disrupted nighttime sleep also are commonly described.

Unwanted episodes of sleep recur several times a day –not only under favorable circumstances, such as during monotonous sedentary activity or after a heavy meal. The duration of the episode may vary from a few minutes, if the subject is in an uncomfortable position, to longer than 1h if the subject is reclining. Narcoleptics characteristically wake up feeling refreshed, and there is a refractory period of 1 to several hours before the next episode occurs. Apart from sleep episodes, patients may feel drowsy, resulting in poor performance at work, memory lapses, and even gestural, ambulatory or speech automatisms.

Cataplexy is an abrupt and reversible loss of muscle tone, most frequently elicited by emotion such as laughter, anger, or surprise and it may occur in more than 2/3of patients with narcolepsy. It may involve certain muscles or the entire voluntary muscles. Most typically, the jaw sags, the head falls forward, the arms drop to the side, and the knees unlock or buckle. The severity and extend of cataplectic attacks can vary from a state of absolute powerlessness, which seems to involve the entire voluntary musculature, to a limited involvement of certain muscle groups or to no more than a fleeting sensation of weakness extending more or less throughout the body. An attack may consist of only a slight buckling of the knees. Speech may be broken due to intermittent weakness affecting the arytenoids muscles. The duration of each cataplectic attack is highly variable, lasting from a few seconds to 30 min.

Cataplexy is associated with an inhibition of the monosynaptic H-reflex and the multisynaptic tendon reflex. H-reflex activity is fully suppressed physiologically only during REM sleep, which emphasizes the relationship between the motor

inhibitory component of REM sleep and the sudden atonia and areflexia. Muscarinic cholinergic regions of the pontine reticular formation and basal forebrain are sites involved in cataplexy via a multisynaptic descending pathway. An increase in postsynaptic D2 receptors was observed in the amygdale of narcoleptic dogs with impairment of dopamine release, suggesting that an abnormal cholinergic-dopaminergic interaction could underlie the pathophysiology of narcolepsy [43].

Sleep paralysis is a terrifying experience that occurs in the narcoleptic on falling asleep or on awakening. Patients find themselves suddenly unable to move their limbs, to speak, or even to breathe deeply. This state is frequently accompanied by hallucinations. In many episodes the patient may be prey to extreme anxiety associated with the fear of dying. This anxiety is often greatly intensified by the terrifying hallucinations that may accompany the sleep paralysis. The patient usually learns that episodes are brief and benign, rarely lasting longer than 10 min and always ending spontaneously.

Sleep onset, either during daytime sleep episodes or at night, may be unpleasant, with vivid auditory or hypnagogic hallucinations. They often involve vision that consists of simple forms (cycles, parts of objects), which are constant or changing size. Auditory hallucinations are also common, although other senses are seldom involved. Another common type of hallucinations reported at sleep onset involves elementary cenesthopathic feelings, changes in location of body parts or feelings of levitation or extracorporeal experiences that may be quite elaborate. Night sleep is often interrupted by repeated awakenings and sometimes accompanied by terrifying dreams. Patients may complain of trouble falling asleep and staying asleep at night, although they may fall asleep repeatedly during the daytime.

General measures in therapeutic approach are: avoid shift in sleep schedules, avoid heavy meals and alcohol intake, regular time of nocturnal sleep and timing and frequency of the scheduled naps, individualized for each patient.

Medications for sleepiness: The effect of stimulant medications vary widely among patients. Amphetamines (dexedrin) were first proposed as a treatment of EDS in narcolepsy. Methylphenidate (Ritalin) also is used. Modafinil (Vigil, modiodal) has been introduced as a successful treatment for EDS. Tricyclic antidepressants have been used for control of cataplexy. A problem with the stimulants drugs is the development of tolerance over 6- to 12- month period, which requires the switching and periodic discontinuation of drugs. Excessive amount of drugs may induce

schizophrenicpsychosis. The stimulants drugs and the tricyclic antidepressants increase catecholamine levels, and their chronic administration may produce hypertension.

A common disorder known as **restless leg syndrome** (anxietas tibiarum) may regularly delay the sleep onset. Therefore RLS is not one of the core sleep disorders. Patients with RLS usually report dysesthetic sensations when they are at rest. These sensations are generally relieved by agitated motor activity. When symptoms occur, patients move their legs vigorously, flexing, stretching, and crossing them. On rare instances there is no dysesthesia. Symptoms are worse later in the day or at night. Most patients report difficulty falling asleep as both sleepiness and lying down in bed facilitate the occurrence of dysesthesia. Some others fall asleep rapidly but wake up in the middle of the night because of paresthesias, which force them to rise and walk around to relieve the discomfort. The intensity of sensory and motor symptoms can vary greatly. During some periods, motor symptoms may be present several times a day while at other times they may be totally absent [49]. The sudden remissions, lasting for months or even years, are as difficult to explain as the relapses which appear without any apparent reason. In several cases symptoms are present every night and in most patients the severity of symptoms increases with advancing age. Several patients (46,2% men and 22,2% of women also report excessive daytime fatigue or somnolence [50]. RLS is sensitive to a variety of influences. Some times appear or worsen during pregnancy [49], with fatigue, exposure to warm environment or prolonged exposure to cold. In severe cases, depression and suicidal thoughts may arise, but RLS should not be confused with the restlessness of anxious patients. RLS also may be responsible for marital difficulties.

The prevalence of RLS was first estimated by Ekbom [51] to be 5% of the general population. A recent population based questionnaire survey revealed the presence of RLS in 10-15% of the responders. It affects the middle –age population equally men and women.

The syndrome usually is benign but is occasionally a prelude to a peripheral neuropathy, particularly uremic polyneuropathy.

Dopaminergic agents are now considered the treatment of choise for RLS. Several medications have proved helpful, such as l-dopa/carbidopa, pergolide, bromocriptine, benzodiazepine, baclophen, carbamazepine, gabapentin and recently magnesium.

A closely related movement disorder resulting in daytime sleepiness is **periodic leg movements during sleep**. Originally described as 'nocturnal myoclonus', the periodic leg movements are slower than myoclonic jerks. PLMS is best described as rhythmical extensions of the big toe and dorsiflexions of the ankle with occasional flexions of the knee and hip, each movement lasting approximately 0,5 to 5,0 with a frequency of about one every 20-40 sec. PLMS clusters into episodes, each of which lasts several minutes to hours and are more numerous in the first half of the night. Intense movements may cause arousals. The prevalence of PLMS is correlated with age [53], rare in young and common in the elderly, 5% of normal between 30 and 50 years, in 29% of subjects over 50 years old and 44% of subjects aged over 65y and older. According to Bixler, PLMS found to be present in 11% of healthy people [53].

L-Dopa is considered as a therapeutic choice for PLMS. Benzodiazepines and bromocryptine also are used, but are less effective.

PLMS co-occurs with a wide range of sleep–wake complaints, including early sleep onset difficulty, nocturnal awakenings and daytime sleepiness.

3.4. Sleep Disorders Classification

Currently there are two diagnostic schemas for sleep disorders. While overlapping, they are different:

i) DSM-IV is the current nosology for classification of mental disorders in psychiatry. The DSM-IV is an axial coding scheme for mental disorders with some sleep disorders. It is not very much used in sleep medicine any longer since most coding schemes should be linked to the ICD and not to axial systems.

ii) The International Classification of Sleep Disorders had been developed by the American Sleep Disorders Association together with other world sleep societies such as the European Sleep Research Society first in 1990 and in revised form in 1997 and 2000. It offers definitions and diagnostic severity criteria for all sleep disorders.

ICD-9-CM (International Code of Diseases) and the ICD-10 (that has specifically allocated room for sleep disorders) are also used but less frequently.

The earliest classification systems were primarily symptom based, and they formed the basis for the modern classification. In 1990 the International Classification of Sleep Disorders was produced after a 5-year process initiated by the American

Sleep Disorders Association. This classification replaced the Diagnostic Classification of Sleep and Arousal Disorders that was published in 1979 [54]. The ICSD development process involved the three major international sleep societies at that time – the European Sleep Research Society, the Japanese Society of Sleep Research, and the Latin American Sleep Society- and resulted in the production of a diagnostic and coding manual, the International Classification of Sleep Disorders: Diagnostic and Coding Manual [42]. A revised version of the ICSD with minor revisions to the text was produced in 1997 [55]. Another update was prepared for 2001 [4]. Currently a major revison of the ICSD is processed. Again delegates from Europe and other sleep research societies in the world participated. This major revision was subject for public comment during July 2004. The revised version of the ICSD, entitled ICSD-2 will be published in 2005 and will be presented to the public during the American Professional Sleep Societies (APSS) conference in June 2005.

The ICSD classification was developed primarily for diagnostic and clinical purposes so that sleep disorders can be defined and morbidity and mortality information could be recorded and retrieved. The classification manual lists 84 sleep disorders, presented in detail with a descriptive diagnostic text that includes specific diagnostic and severity criteria. The ICSD also contains a differential diagnostic listing of the sleep disorders. This listing is presented in order to assist the new clinician in using the three major sleep symptoms: insomnia, excessive sleepiness, or an abnormal event during sleep for diagnosis.

The ICSD is structured into four categories: (a) the dyssomnias, which are disorders of initiating and maintaining sleep and the disorders of excessive sleepiness; (b) the parasomnias, which are disorders that may cause a complaint of insomnia or excessive sleepiness; (c) disorders associated with medical or psychiatric disorders, and (d) the proposed sleep disorders, which are disorders for which there is insufficient information to confirm their acceptance in the sleep community as a definitive sleep disorder. This last category was required because of the rapid advance of sleep medicine that resulted in the discovery of several new sleep disorders.

However, it is noticed that there is much variability in our knowledge of sleep disorders. For some sleep disorders, such as narcolepsy and sleep apnea, a large body of research and literature exists. For other sleep disorders, there is barely enough evidence to document that they exist. Given the wide variability in our knowledge about individual sleep disorders, the quest for a common framework along which to

sort all the sleep disorders had to be abandoned. Rather, ICSD-2 sorted the sleep disorders into eight categories that appeared to make most pragmatic and empirical sense at the current time. Thus, some groupings are based on a common complaint (e.g. insomnia or hypersomnia). Others are based on a presumed basic etiology (e.g. biological clock disturbances for circadian rhythm sleep disorders). Still others are grouped according to the organ system from which the problems arise (e.g. sleep related breathing disorders).

A description of the proposed ICSD-2 classification is included in APPENDIX III, however it is not published today. It has been therefore agreed during the focus group meeting in 2004 that in the current project the ICSD classification (APPENDIX III) will be followed.

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4. Distance monitoring applications in sleep disorders

A distance monitoring system is a remote telemetry system that allows making a follow up of the patient from a distance. An example of distance monitoring is home monitoring where patient is monitored from his/her own home, thus allowing sleep specialists to analyze in the distance, the evolution of the patient.

In SENSATION we will not be limited in home monitoring applications. We aim to realize distance monitoring applications that enable the 'anytime, anywhere' physiological monitoring of patients. This section presents the current status of distance monitoring in the treatment of sleep disorders.

4.1. The role of distance monitoring in sleep disorders studies

Polysomnography (PSG) is a diagnostic procedure used for sleep disorders. In practice, it provides a very comprehensive assessment of patients sleep patterns, including the effects of various medications, physical, psychological and / or sleep related disturbances. PSG is a multifaceted field, which reveals critical information regarding sleep physiology. In one clear arranged package you see all parameters in parallel and changes can be correlated with each other. With PSG, multiple physiological variables during sleep are recorded: EEG, EOG, EMG, ECG, respiration. The term Cardiorespiratory PSG is often used when ECG and respiration are included.

Cardiorespiratory polysomnography and MSLT in a sleep laboratory are the recognized golden standards for sleep investigation studies, and particularly for sleep related breathing disorders [56]. During cardiorespiratory polysomnography study in a sleep laboratory, patient spends a full night at the lab. A specialized sleep technician assists patient, helps with the setting and usage of the equipment and observes him/her during sleep. In addition to the PSG physiological variables, sleep technician may provide input with observations that can contribute in the diagnosis (e.g. observations on patient behavior, psychological problems). However, PSG is labor-intensive and time consuming and requires technical expertise. Timely access is also a problem for

many patients, the majority of whom continue to have undiagnosed sleep disorders. Furthermore, not many sleep centers are available.

Due to the high cost of PSG studies and limited availability of sleep labs, there is high interest in the role of simplified, unattended sleep monitoring for sleep related breathing disorders that would allow the patient to be studied at home, rather than in the sleep laboratory.

Most portable systems for in-home assessment of sleep disorders described in the literature have been developed and evaluated for OSA applications. Only one was found during our literature search for Periodic Limb Movement [58].

Advances in microtechnology during the last decades have resulted in the development of sleep recording systems that enable remote physiological monitoring. The terms “ambulatory sleep recording” or “portable monitoring” have been used for such methods. Technical differences between polysomnography systems compared to ambulatory systems have become so small; that the same recording equipment can be used for both sleep laboratory settings and outpatient use [56]. Thus, the role of ambulatory sleep recording has shifted from the question of what is technically feasible to that of the strategies involved. Moreover, many researchers have doubted portable monitoring systems’ reliability. An increasing amount of research has been published comparing some type of portable monitoring for sleep apnea with polysomnography. A systematic review of the literature focus on home diagnosis of sleep apnea could be found [59].

Applications of distance monitoring in sleep disorders are focused on the development of methods that enable in-home assessment of sleep. The main reason for developing such methods has been the need for alternative approaches to the laboratory based polysomnography exam. Ambulatory recording of sleep related breathing disorders using a reduced number of parameters is important and useful in many cases with a clear-cut risk profile for sleep related breathing disorders. Ambulatory sleep recording is also very useful for annual treatment control studies in patients with sleep related breathing disorders under ventilation therapy. In addition, ambulatory recording of sleep with complete polysomnography is useful in occupational medicine, research studies, space research, and for special questions, which cannot be addressed in a fixed sleep laboratory.

Therefore, procedures that enable in-home assessment of sleep are needed in order to:

- Reduce the long waiting lists in sleep labs.
- Reduce the cost of a very expensive exam (about 390 euros per session).
- Enable sleep investigations in areas where no sleep lab is available.
- Allow for a more comfortable exam where patient does not have to spend a whole night at a hospital, but can sleep at his/her own home.

4.2. Assessment of sleepiness and performance

Daytime sleepiness and performance are currently only measured in lab environment and established methods are the following:

a. Self-reports

They include a number of developed scales ranging from the Stanford Sleepiness Scale, Epworth Sleepiness Scale, Sleep-Wake Activity Inventory, Karolinska Sleepiness Scale, and a variety of 100-mm linear scales. The most widely used are Epworth Sleepiness Scale (ESS) and Karolinska Sleepiness Scale (KSS).

ESS is a simple widely used, self-administered questionnaire, which is shown to provide a measurement of the subject's general level of daytime sleepiness [110]. It asks a person to rate the likelihood that he or she would doze off or fall asleep during eight various everyday activities such as reading a book, riding as a passenger in a car for an extended period of time or taking a nap in the afternoon. Scoring is based on a scale ranging from 0 to 3: 0 means a person would never doze during the activity; and 3 means there is a very high chance that a person would doze during that activity. Add together all the answers to get a score; the ESS has a possible score range of 0 to 24.

- A total score of less than 10 suggests that a person is not suffering from excessive sleepiness.
- People who do not experience excessive sleepiness score about 5.9.
- People with obstructive sleep apnea treated with CPAP score about 11.7.
- People with untreated obstructive sleep apnea score about 16.0.
- People with Parkinson's disease score about 16.9.
- People with narcolepsy score about 17.5.

KSS is a commonly used tool to measure levels of sleepiness and is a nine-point scale that ranges from 1 = very alert to 9 = very sleepy, great effort to stay

awake or fighting sleep. Patients are asked to rate their sleepiness in the five minutes prior to taking the test.

b. Physiological measurements

Physiological measurements, at least in principle, should be more amenable to objective measurement and free from reporting biases. The Multiple Sleep Latency Test (MSLT) and Maintenance of Wakefulness Test (MWT) represent two of the most widely accepted measurements.

MSLT is often referred to as the "gold standard" for measuring sleepiness. It is an objective test designed to measure how quickly patients are able to fall asleep [60]. Patients are instructed to lie down in a dark room without any extraneous stimuli and attempt to sleep. Polysomnographic measures are then administered to record sleep latency (the number of minutes required to fall asleep). Each test session is 20 minutes long; the first test is administered two hours following nocturnal PSG. The MSLT is subsequently administered fours times throughout the day at two-hour intervals and the mean value of the four tests is utilized. Normal time for sleep onset to occur is 10 minutes or longer.

- A person who is not sleep-deprived typically will have a sleep latency greater than 15 minutes.
- A person who has mild sleepiness will have a 10 to 15 minute sleep latency.
- A person with significant sleepiness will have a mean sleep latency of 5 to 10 minutes.
- A person with pathologic sleepiness will have a mean sleep latency of less than 5 minutes.

MWT is an objective test of the ability to resist sleep when instructed to remain awake while reclining in a dark, quiet room for 20 minutes. The MWT is a daytime study, generally conducted following the evening of the PSG study. It generally begins two hours after the patient's normal rise time and involves a series of four to five tests at set intervals throughout the day. Patients are monitored during this test using most of the same recording equipment used during the PSG tests.

c. Behavioural Tests

They include simple repetitive performance tasks or reaction tests, such as PVT and OSLER test.

PVT (Psychomotor Vigilance Test) is a test of behavioural alertness and sleepiness that measures sustained attention and reaction time in response to a randomly occurring flash over a 20-minute period. The PVT is a research tool that attempts to standardize and quantify the impact of sleepiness.

OSLER test simplifies the performance of MWT. In this test, the occurrence of sleep is assessed behaviourally rather than by EEG monitoring. The subject is asked to respond by hitting a button each time a dim light flashes. The light-emitting diode flashes regularly for 1 second every 3 seconds. The subject is instructed to remain awake in this soporific situation for a maximum testing time of 40 minutes. When the subject fails to respond for 21 seconds, the test is ended and it is assumed that the patient has fallen asleep. Thus, the OSLER test reproduces many of the MWT characteristics, with the advantage of being a simpler and less expensive tool, which does not require the presence of a trained technician. The simplicity of the test makes it easy to be used outside the sleep laboratory setting. The OSLER test has been also confirmed as a strong indicator of daytime sleepiness in patients with OSAS [61].

Other less commonly used methods but with great potential for ambulatory application are extent of eyelid closure and blink speed [62]. Actigraphy has been evaluated positive in space research both as a way of detecting bedtimes and waketimes, and as an indicant of sleep restlessness [63]. Alpha band topographic changes (frequency domain) could be a factor that could be linked with the drowsiness, but is not evidenced yet [116].

4.3. Systems Development

The term portable monitoring encompasses a wide rage of devices that can record as many signals as does attended polysomnography or only one signal, such as oximetry. Over the last years, there have been considerable advances in ambulatory monitoring of sleep and it is investigated whether it could be used instead of PSG.

Ambulatory sleep recording started with long-term EEG recording in the mild-70s. Many long-term recorders were built using the Oxford Medilog 4-24 recorders [64]. Most sleep disorders required the recording of other signals beside EEG. The first sleep recording systems were developed as already existing EEG systems expansions. Technical advantages in microtechnology have enabled the development of sensors that record respiratory, cardiovascular and body movement data. These

sensors are embedded into portable sleep monitoring devices that can record and save in memory the signal data that can afterwards be retrieved via special software. Microprocessors development allowed to heart rate and respiratory rate calculations. Vitalog PMS-8 was a pioneer system that used the new technology [65]. Nowadays, digital systems range from one-channel recorders to reduced channel sleep recording with 4 to 8 signals to multi-channel sleep recording with 10 or more signals. Most of the portable devices now, offer the option of automated classification algorithms for diagnosis, however in most cases visual analysis by the physicians is preferred.

4.4. Sleep recording measurements and breathing events detection

A standard PSG typically consists of 2 channels electroencephalogram (EEG), segmental (+/-) electromyogram (EMG), electrooculogram (EOG), respiratory airflow (usually measured by oronasal flow monitors), thoraco-abdominal movement and oxygen saturation tracings (oximetry). Electrocardiogram (ECG) and body position are also frequently monitored, as is snoring (Table 1). Recently, PAT (Peripheral Arterial Tone) was used for sleep disorders evaluation.

Most monitors focus on breathing events (apnea/hypopnea) detection and evaluation. As with polysomnography, there was heterogeneity with respect to defining an abnormal breathing event on a portable monitor. The most common methods to detect breathing events were reduction in airflow measured by a thermistor or by a nasal pressure signal [59]. The best method for quantifying airflow is pneumotachograph. Some portable monitors use this technology. Four types of measurements have been used in order to define an abnormal breathing event:

a. Flow

A reduction in airflow or tidal volume is the standard method for defining an apnea or hypopnea. A criterion for defining an hypopnea has been recommended to be reduction to <50% from baseline of a valid measurement [66]. Thermistors sense differences in temperature and although they do not have a linear relationship with true airflow, they remain the most common method for defining breathing events. Therefore, they may not be sensitive for detecting hypopneas [66]. Nasal pressure provides a linear approximation of airflow across its complete range except at extremes. It may be as accurate as a thermistor in distinguishing an apnea from a hypopnea; however, in routine clinical use this distinction is not thought to be so

important. The signal could produce false-positive events if the patient was mouth breathing for long periods of time. This may require visual confirmation of apparent apnoeas and hypopneas, making it potentially difficult to use in an unattended study [67], [68].

b. Respiratory inductance plethysmography (RIP)

RIP can provide a measure of tidal volume. It is used primarily during polysomnography. It has been used in only one study on portable monitoring as a secondary signal.

c. Oxygen saturation

Most methods rely on the detection of a drop in oxygen saturation; some detect resaturation, while others use both criteria. Some automated analyses define what baseline oxygen saturation is, but most do not. Some studies have measured the percentage of cumulative time that a patient has an oxygen saturation of <90% to determine whether it identifies patients with sleep apnea [66].

One report used snoring as a primary method for event detection and combined it with oxygen desaturation as a second required criterion for event detection [69]. Other studies have used snoring in conjunction with heart rate variability as criteria for event detection [70], [71]. Spectral analysis of heart rate was used in one study [72]. Pharyngoesophageal pressure measurement has also been used by one study as a method for detecting breathing events [73].

d. Peripheral Arterial Tone (PAT)

PAT signal is a measurement of the pulsative volume changes in the fingertip arteries which reflects the relative state of the arterial vasomotor activity, and thus indirectly the level of sympathetic activation [74]. WP 100 device can measure the PAT signal [75]. The zzzPAT algorithms use the four WP 100's channels (PAT, pulse rate, oxygen saturation, and actigraphy) for the detection of respiratory events and arousals from sleep. More specifically, PAT respiratory disorders index and PAT arousals index have been proposed for abnormal breathing events evaluation [76]. Evaluation studies have shown [112] that WP100 device is well suited to perform therapy control studies in patients suffering from sleep apnea and being treated.

Respiration:	Airflow CPAP pressure Respiratory effort Snoring sound Oxygen Saturation
Cardiovascular:	ECG Heart Rate Peripheral Arterial Tone
Sleep:	EEG EOG EMG
Movement:	Body position Acceleration

Table 1: The vital signs that are usually recorded during PSG.

4.5. Systems Classification

Portable ambulatory sleep recording systems were classified according to the approach used in the 1994 American Sleep Disorders Association review [77]. Four types of ambulatory sleep recording systems have been classified (Table 2):

a. Type I (standard polysomnography)

Type I was considered the reference standard to which the other monitor types were compared (Table 3). The physiological signals that were recorded and used to define a breathing event on a portable monitor varied among studies and across monitor types [78]. Type I devices are portable in the sense that patients at their homes can use them. However, attachment of the electrodes needs to be done by a specialist at patient's home. The specialist also needs to de-attach the electrodes therefore the cost of the exam increases significantly.

b. Type II (comprehensive portable polysomnography)

Type II monitors incorporate a minimum of seven channels, including EEG, electrooculogram, chin EMG, ECG or heart rate, airflow, respiratory effort, and oxygen saturation (Table 4). This type of monitor allows for sleep staging and therefore for the calculation of an Apnea-Hypopnea Index (AHI). Type II devices, as Type I can be used at patient's home but electrodes attachment has to be done by a specialist.

c. Type III (modified portable sleep apnea testing)

Type III monitors incorporate a minimum of four monitored channels, including ventilation or airflow, heart rate or ECG, and oxygen saturation (Table 5.

Type of Portable Monitoring Device	**Parameters Measured**
Type I PSG	More than 10 channels
Type II Comprehensive Portable	Polysomnography Minimum of 7 channels, including EEG, EOG, chin EMG, ECG or heart rate, airflow, Respiratory effort, and oxygen saturation
Type III Modified Portable Sleep Apnea Testing	Minimum of 4 channels monitored, including ventilation or airflow (at least 2 channels of respiratory movement, or respiratory movement and airflow), heart rate or electrocardiogram, and oxygen saturation
Type IV Continuous Single or Dual Bioparameters	One or 2 channels, typically including oxygen saturation or airflow

Table 2: Ambulatory Sleep Recording Systems Classification according to American Sleep Disorders Association review.

d. Type IV (continuous signal or dual bioparameters)

Most monitors of this type measure use a single parameter or two parameters, for example oxygen saturation and overflow (Table 6). A monitor that did not meet the criteria for type III (ie, a monitor that measured one to three channels or did not include airflow despite having four channels) was classified as Type IV. The majority of these devices does not include electroencephalography and, therefore cannot reliably record or evaluate sleep staging. Monitoring of sleep stages through EEG is feasible by devices such as BioSomnia and Quisi. BioSomnia Plus is another portable device that uses a single EEG channel and also provides a sleep hypnogram. No evaluation studies have been reported in the literature for BioSomnia and BioSomnia Plus. Quisi [79] enables the recording of one channel EEG, one channel EMG and one channel EOG. These three signals are then combined in a hypnogram. However, this device does not give the original signals (raw data) and has not been proven useful. In Type IV category, the recently developed device Watch-PAT 100 could be classified, that measures continuously the Peripheral Arterial Tone (PAT) signal, pulse rate, oxygen saturation and actigraphy [75]. Watch-PAT 100 provides automatically sleep-wake events, and PREM (PAT REM) events using four channels of PAT, pulse rate,

oxygen saturation, and actigraphy. These devices are discussed in more details in the following chapter.

4.6. Systems Presentation

Portable devices that are currently available in the market are listed in tables 3, 4, 5, and 6, classified according to the types mentioned above.

Quisi has been developed as a one-channel, self-applicable ambulatory EEG recording device with three electrodes placed on the forehead, using neuronal networks techniques for automatic sleep stage classification (Figure 1 – Table 7). Quisi allows detailed information about TST, sleep efficieny and structures of sleep profile. Quisi gives an impression of sleep architecture and objective verification of a sleep disturbance in an ambulant setting but cannot replace the sleep laboratory-based PSG [79].

Figure 1: Quisi electrodes for EEG recording.

Oxford BioSignals has introduced the BioSomnia portable sleep system (Figure 2 – Table 6). Developed from leading edge neural network technology, BioSomnia is the first single EEG channel sleep system to provide information on the quantity and quality of sleep. BioSomnia is a lightweight, battery-powered portable monitor processing a single channel of EEG overnight. No validation studies were found in the literature for this device.

SOMNOcheck is an ambulatory device for sleep apnea diagnosis and therapy monitoring (Figure 2). This device measures respiratory flow, snoring noises, pulse rate, oxygen saturation, body position and nCPAP pressure. SOMNOcheck has showed a very high diagnostic accuracy for the diagnosis of OSA and was able to define its severity precisely [80]. The diagnostic accuracy of manual analysis was found to be superior to that of automatic analysis [80]. Considering the results of this

technical evaluation [80], the SC may also be expected to work reliably when it is used in an ambulatory setting.

The Embletta PDS (Portable Diagnostic System) is a pocket-sized digital recording device that has been designed for the diagnosis of sleep-disordered breathing (Figure 2). It records nine physiological channels. Embletta PDS's memory records up to twelve hours of comprehensive respiratory data that can be easily reviewed and analyzed using SomnologicaT for Embletta software. Most patients were satisfactorily classified by home Embletta studies some of them required further investigation [81]. A validation study suggested a 42% saving in diagnostic costs over polysomnography if this approach were adopted [81]. The XactTrace Respiratory Inductive Plethysmograph (RIP) is an important addition to the Embletta system because it delivers respiratory effort tracing. The Xact-LM Extension proxy for the Embletta has been designed for users that want Limb Movement information included in their Embletta sleep study. However, no evaluation studies of this device have been found in the literature for Periodic Limb Movement disorder.

Watch-PAT 100 is an ambulatory unattended diagnostic device for sleep related breathing disorders. The WP100 is worn on the wrist and is utilising a plethysmographic based finger-mounted probe, to measure the PAT (Peripheral Arterial Tone) signal. Automatic analysis of peripheral arterial tonometry signal derived from the ambulatory device Watch-PAT100 can accurately identify arousals from sleep in a simple and time saving fashion [75]. Moreover, WP100 may offer an accurate, robust, and reliable ambulatory method for the detection of OSAS, with minimal patient discomfort [76].

The NovaSom QSG consists of a bedside console and three small sensors, which are easily applied by the patient before going to sleep, following simple instructions and voice prompts. The system can be used for up to three nights to collect sleep data, including respiratory events (apneas and hypopneas), snoring intensity, blood oxygen saturation, pulse rate and respiratory effort. In a patient population suspected of having OSA, the NovaSom QSG demonstrated acceptable sensitivity and specificity both in the lab and self-administered in the home, when compared to PSG [82].

The MERLIN device is a useful diagnostic approach for the initial assessment of adult patients with clinical suspicion of sleep apnoea/hypopnoea syndrome. Manual scoring is clearly better than automatic scoring in terms of agreement with the

apnoea/hypopnoea index and to discern patients with sleep apnoea/hypopnoea syndrome [83].

		
BioSomnia	**SOMNOcheck**	**Embletta PDS**

Figure 2: Three typical ambulatory sleep-recording systems.

Device	Parameters	Characteristics	Evaluation - Validation
Medcare Embla S7000	12 Referential channels 8 bipolar channels 9 respiratory channels	Ambulatory device for sleep centers	No evaluation listed in Medline
Compumedics E-Series	20 EEG 2 EMG 2 EOG 3 ECG Oronasal air flow Thoracoabdominal movements Oxygen saturation	Connected with a Network-Linked Amplifier System	No evaluation listed in Medline
Compumedics Siesta	32 channels	1. Wireless Data Transmission or 2. Record raw data to a Compact Flash Card	No evaluation listed in Medline

Table 3: Currently available systems of type I.

Device	Parameters	Characteristics	Evaluation - Validation
Minisomno	two EEG one EMG one EOG one ECG oronasal air flow thoracoabdominal movements oxygen saturation	8-18 channels can equip with a modem	[87]
Oxford Medilog	8 channels	Appropriate for periodic leg movements analysis Sleep Stages Automatic Analysis	[88], [113], [114]
Compumedics Somté	2 channels of EOG, EEG, EMG, or ECG. Pressure Airflow Snore Thoracic Effort Abdominal Effort Limb movement Body position SaO_2 Pulse rate Pulse waveform		[98]
DigiTrace			[97]
Embla A10	Polysomnography 16-17 channels event channel two oximeter channels	On-line polysomnographic recorder, or an ambulatory EEG recorder	No evaluation listed in Medline

Table 4: Currently available systems of type II.

Device Name	Parameters	Characteristics	Evaluation - References
Somnocheck	4 channels Airflow CPAP Snoring sound SaO_2 Heart rate Body position	Sleep Apnea diagnosis and follow-up. Self-applicable by patient.	[80]
Embletta	8 channels Flow/Pressure Nasal/Oral flow Snore Abdominal & Chest wall movement Oximetry Pulse Rate Body Position Activity meter Flow limitation		[81]
Edentrace	4-6 channels Heart rate, Body position oronasal flow chest impedance breathing noises pulse oximetry		[103], [104]
PolyG	ECG, Body position oronasal flow chest wall & abdominal movement oximetry		[100]
Merlin	4-6 channels Airflow CPAP Respiratory effort Snoring sound SaO_2 Heart rate Body position	Going out of the market now Provides better risk estimate for in patients with sleep related breathing disorders and cardiovascular disorders such as CHF.	[103], [90]
Digitrapper	4-6 channels		[91]

Table 5: Currently available systems of type III.

Device	Parameters	Characteristics	Evaluation - References
Quisi	one-channel self-applicable ambulatory EEG	Only hypnogram Sleep staging	[79]
BioSomnia	One EEG channel	Only sleep parameters Neural network technology for sleep staging estimation	No evaluation listed in Medline
Watch PAT-100	PAT Pulse rate Oxygen saturation Actigraphy	Unattended diagnostic device	[75], [76], [112]
MESAM4	4 channels Snoring sound SaO2, Heart rate Body position	Reliable for diagnosis and therapy control of sleep related breathing disorders	[70], [71], [84], [85], [86]
Actiwatch	Digitally integrated measure of gross motor activity	Specialized for Periodic Limb Movement diagnosis	[94], [93]

Table 6: Currently available systems of type IV.

Device	Parameters	Characteristics	Evaluation - References
Quisi	EEG (1channel) EOG (1channel) EMG (1channel)	Only hypnogram, no raw data available	[79]
Biosomnia	EEG (1Channel)	Only sleep parameters	No evaluation listed in Medline

Table 7: Currently available systems for EEG recording.

The MESAM 4 device records oxygen saturation using finger pulse oximetry, snoring using an electric subminiature microphone placed over the larynx, beat-to-beat, heart rate analysis and body position using a circular sensor taped just below the sternum. The MESAM 4 device is a validated tool in epidemiological research and clinical routine [84]. Automatic analysis of MESAM 4 recordings may be misleading in evaluating OSA patients who have a fall in baseline SaO_2 during sleep. In this case, visual scoring performed by a trained polysomnographer is recommended [85], [86].

Minisomno is a portable device, weighing 660 g, able to record and store 8 h of data from 8 to 18 channels. It is the portable version of the Respisomnographe (Mallinckrodt). The Minisomno can equip with a modem adapted to the frequency of the signals recorded and to the telephone network. This modem allowed periodic televisualization of the signals recorded (two EEG, one chin electromyogram (EMG), one electrooculogram (EOG), oronasal air flow via thermistors, thoracoabdominal movements, arterial oxygen saturation, and ECG, and, at the end of the night, teletransmission of the recordings performed in telemonitored centers for analysis by the telemonitoring center. According to Portier et al who compare home polysomnography (HoSD) with laboratory polysomnography in the diagnosis of sleep apnea syndrome (SAS) by using Minisomno portable device, the reliability of HoSD-PSG for SAS diagnosis depends on the quality of data obtained under unattended conditions [87].

4.7. Systems Validation

Several approaches can be used to validate portable monitoring. The standard approach has been to compare portable monitoring with a reference standard that used to be PSG [56]. The limitation of this approach is that it assumes that sleep laboratory-based PSG is the optimal approach for diagnosing sleep apnea. However, this is not completely true because patients frequently do not sleep as well in a sleep lab as they do at home [59].

Evaluation can be done in an attended setting (most often in a sleep laboratory) or in an unattended setting (most often at patient's home). The evaluation of a portable monitor in an attended setting allows an assessment of its performance under ideal circumstances eliminating important sources of possible differences that have nothing to do with the portable monitor, such as, differences in the conditions of sleep between laboratory and home environments and night-to-night variability.

Several methods exist for evaluating the extent of agreement between two methods designed to measure the same phenomenon. The methods reported in the literature for comparing the results of portable monitors and polysomnography include Pearson correlation coefficient, interclass correlation coefficient, the approach of Bland and Altman of mean differences and limits of agreement, and sensitivity/specificity/likelihood ratios (LRs) [95], [96].

4.7.1. Validation Studies of Portable Monitors investigating OSA

A systematic review of portable monitoring for investigating adults with suspected sleep apnea was performed by Flemons et al [59] in 2003. This work resulted to the generation of Practice Parameters for the Use of Portable Monitoring Devices in the Investigation of Suspected Obstructive Sleep Apnea in Adults, by the American Academy of Sleep Medicine, the American Thoracic Society and the American College of Chest Physicians [57], concluding that home studies using portable devices are not reliable. However, many such devices are used for every day clinical practice and clinicians are satisfied with their use. Such devices give the clinician the opportunity for a polysomnography measurement at patients home. On the other hand, in about 50% of the clinical cases, there is a need of an additional PSG exam at the sleep center [94].

Type II monitors allow for sleep staging and should give the best agreement with polysomnography because an AHI can be calculated [97], [87], [98]. However, the number of studies is very limited and they cannot provide convincing evidence indicating that type II monitors could be used in either an attended or an unattended setting [59].

Several studies with a high level of evidence and high quality consistently show that some type III monitors can successfully be used to rule out sleep apnea (decrease the probability of sleep apnea) in an attended setting [91], [104], [100]. In an unattended setting, the results should be considered preliminary and suggest that these monitors may be useful, but that their actual usefulness requires additional studies. There are several high-quality studies showing that type III monitors can be used to rule in sleep apnea (increase the probability of sleep apnea diagnosis) in an attended setting [80], [91], [103]. The data supporting their usefulness for ruling sleep apnea in the unattended setting are limited. Overall, the most consistent, high-quality data were for type III monitors in the attended setting, where they had been proven to either confirm or exclude sleep apnea in a sleep laboratory population. The number of false results was low in these studies, and the majority of studies were able to find one cutoff RDI, that allowed distinction between patients with and without sleep apnea [104], [105].

Oximetry alone can be used to rule out sleep apnea both in an attended and unattended setting. However, in the latter situation the results should be considered as

preliminary [101]. The addition of a second signal showed results that were similar to those using oximetry alone, and similar conclusions can be drawn. Nasal pressure may be useful in an attended setting, but no conclusions can be made about its use in an unattended setting [67], [102]. Moreover, Peripheral Arterial Tone (PAT) may offer an accurate, robust, and reliable ambulatory method for the detection of OSAS, with minimal patient discomfort [75], [76], [112].

4.7.2. Validation Studies of Portable Monitors investigating other sleep disorders

Validation studies of portable monitors for other sleep disorders are very limited.

KickStrip and Oxford Medilog monitors have been evaluated for Periodic Limb Movement diagnosis for both clinical and research purposes [58], [64]. The advantages of ambulatory PSG recordings by using Oxford Medilog monitor in insomnia children have been discussed by Plouin et al. [113] and Saletu et al. [114]. Actiwatch device was used in order actigraphy method to be evaluated for assessing hypnotic effects of insomnia [115].

4.8. Existing guidelines in the use of portable monitoring for sleep disorders

Guidelines on the use of portable monitoring were issued between 1994 and 1999 by a number of authors, including the American Academy of Sleep Medicine, the Agency for Health Care Research and Quality, and the Emergency Care Research Institute [106], [107], [108]. Although differences in analysis techniques and classification of portable monitoring devices exist among these studies, uniformital recommendations have been issued.

The final outcome of a collaboration of the American Thoracic Society (ATS), the American Academy of Sleep Medicine (AASM), and the American College of Chest Physicians (ACCP) on establishing standards and guidelines for portable monitoring was three publications. According to these studies:

(1) Insufficient evidence is available to recommend the use of Type II PM devices in attended or unattended settings.

(2) Type III PM devices appear to be capable of being used in an attended setting to increase or to decrease the probability that a patient has an apnea-hypopnea index greater than 15.

(3) The use of Type III PM devices in an unattended setting is not recommended to rule in, rule out, or both rule in and rule out a diagnosis of OSA.

(4) There is some evidence that the use of Type III PM devices in an attended in-laboratory setting may be acceptable to both rule in and rule out a diagnosis of OSA if certain limitations are in place. These limitations include manually scoring the records, using the devices only in patients without significant comorbid conditions, having awareness that symptomatic patients with a negative study should have a Type I study, and not using these devices for titrating positive airway pressure or conducting split-night studies.

(5) The use of Type IV PM devices in attended or unattended settings is not recommended.

Therefore, according to these guidelines, the use of Portable Monitoring in the US is not recommended in the unattended setting in the current clinical practice. No official guidelines have been published in Europe.

4.9. Re-imbursement policies for sleep studies and political implications in Europe

In Europe, each country has a different re-imbursement policy for obstructive sleep apnea diagnosis and treatment. Re-imbursement policies in each country play a crucial role in the use of such equipment, both in the type of equipment that will be used and in the type of investigation that it will be used for. For example, in Germany, the cost for a three-night lab exam is about 1000 Euros whereas the cost of an ambulatory home exam is estimated to be 150 euros. However, re-imbursement is only 30 Euros for an ambulatory home exam. This limited amount automatically restricts the physicians to the use of portable devices with 4, maximum, number of channels. These devices are then used mainly for ruling out patients suspected to have OSA. Re-imbursement for apnea treatment is received only when obstructive sleep apnea is being diagnosed in a sleep lab with a PSG. As a result of this policy, devices

with 8 or more channels that could offer much more information to the clinicians, are not used.

No official guidelines exist in Greece about the use of portable devices and re-imbursement is given for ambulatory exams in the unattended setting. This definitely constitutes a problem since, their use depend on the degree of training and expertise of the referring physician.

In France, there is no official guideline defining in which situations a PSG at the lab should be performed or at home through a portable device. It is up to the physician to decide if an in-home exam is required and then the prescribed exam is reimbursed. However, if obstructive sleep apnea diagnosis is performed through portable devices, without EEG monitoring, then re-imbursement of obstructive sleep apnoea treatment can be obtained only if AHI is very high. But, according to the French law, if an AHI of less than 30 per sleep hour is observed then to obtain re-imbursement a PSG record has to be done. If in this new record the concomitant EEG shows a microarousal index (linked to respiratory events) of more than 10 per sleep hour a re-imbursement can be obtained.

It is clear that the use of portable equipment in the unattended setting depends not only on what technology offers but also on the official guidelines and even more on the re-imbursement policies that exist in each country.

5. Proposed SENSATION medical applications

5.1 Clinical Problems Selection Criteria

SENSATION aims to apply novel micro and nano sensors and related technologies, for low-cost and high-efficiency physiological state monitoring. The focus of the work is the brain activity, including the sleep and wakefulness states and their transitions, stress, inattention and sub-vigil states, for sub-vigilance detection, prediction and management as well as diagnosis, treatment and remote monitoring of sleep disorders. Therefore, in SP3, the medical applications that will be realized and tested will allow remote physiological monitoring for patients who suffer from a sleep disorder, and/or show daytime symptoms such as excessive daytime sleepiness, drowsiness, stress, inattention, etc.

The criteria for selecting clinical conditions that will be remotely monitored through the SENSATION medical applications are listed below:

- Relevance with sleep/wakefulness, excessive day sleepiness, sub-vigil states, drowsiness, stress, inattention
- Need of physiological monitoring
- Currently high cost in the diagnosis and treatment of this condition, and need to develop more cost-effective methods through distance monitoring
- Possibility of improving the quality of current procedures, through distance monitoring, in terms of reliability, patient and clinician satisfaction and comfort.
- Availability of sensors that would enable ambulatory monitoring of this condition (this information is not currently available)
- Expertise in these disorders from SP3 clinical partners
- High prevalence of this condition

At this point the selection of clinical conditions has not been finalized. However, in the current chapter we present proposed clinical conditions, the reasons they have been proposed, their treatment variables, and initial requirements for the medical applications to be realized. This material constitutes the basis for the

interviews and focus groups in the following 6 months, with the aim to provide medical applications scenarios and user requirements by project month 12.

5.2. Sleep related clinical conditions proposed for distance monitoring

OSA and insomnia have been proposed during the interviews and focus group as sleep disorders that would benefit from development of distance monitoring methods due to their high prevalence in the population. Specifically, in-home diagnosis of patients with OSA and treatment evaluation of patients with insomnia could be medical applications that will be realized and tested in SP3.

It has been established by research that OSA is the main cause of excessive daytime sleepiness and has a high prevalence (4% in men and 2%) [99]. Excessive Daytime Sleepiness is an unspecific complaint and also a symptom of many other sleep disorders, such as: central sleep apnea (CSA), narcolepsy, idiopathic, post traumatic and recurrent hypersomnia, periodic limb movement disorder (PLMD) [4], restless legs syndrome [50]. However, these disorders are less frequent. According to the International Classification of Sleep Disorders (ICSD), physiological monitoring, i.e. a cardiorespiratory polysomnography (PSG), is required for OSA diagnosis [4]. In fact, OSA evaluation is the most frequent reason for a PSG investigation in a sleep lab. The cost of a PSG exam is high (approximately 1000 Euros) and it can only be performed in sleep labs due to requirement of attending personnel. In-home assessment of OSA could result in considerable cost savings, improvements in patient comfort, reduction of long waiting lists in sleep labs, therefore SENSATION should contribute to the improvement of these methods by distance monitoring.

As it has already been discussed in chapter 4, some distance-monitoring systems for home based diagnosis for OSA already exist, nevertheless further improvements and validation studies are required (table 10). Main disadvantage is that they are not easy to use; installation of the electrodes is complicated and technician assistance is necessary. Technical artefacts are very frequent due to the fact that patient is unattended while sleeping, and cables may fall off. Data then is non interpretable and the study has to be repeated in the lab. Additionally, all electrodes are cabled to the main device and this disturbs the patients. In order to reduce the number of cables and electrodes, simplified solutions have been developed (Type 3 and Type 4 devices) but can only be used in a few situations for screening only, according to clinician's judgment. SENSATION can improve in-home assessment

techniques, by manufacturing low cost, easy to use sensors and by investigating the use of new signals in order to develop simplified methods to perform diagnosis (e.g. arterial tonometry signal) and by implementing and testing remote monitoring through telecommunication networks.

Insomnia is primarily evaluated by an extensive medical interview, physical examination, additional subjective data (sleep diaries, questionnaires) and sometimes objective measures (PSG, actigraphy). Currently, in clinical practice, the use of polysomnography is not supported for routine evaluation of either transient or chronic insomnia. PSG is, however, essential to diagnose sleep state misperception and to diagnose other sleep disorders that create symptoms of insomnia. PSG would be useful as a repeated measure before and after treatment of insomnia and it is recommended if the improvement of sleep needs to be objectified. SENSATION aims to develop new methods that will allow assessment of insomnia at lower cost. Distance monitoring applications would allow low-cost monitoring for more than one night when needed (the first night effect is a special issue of concern in insomnia).

Proposed applications include the study of daytime consequences of insomnia. Current data suggest that the daytime consequences which are associated with an insomnia complaint may not be due to sleep deprivation but, instead, to hyperarousal which gives rise to both sleep disturbance and waking complaints. With the development of methods that enable patient monitoring during their daily activities and evaluation of this, underlying hyperarousal, SENSATION could highly contribute to research in this area.

The main innovation that SENSATION could achieve and that is not possible through hospital or sleep laboratory based monitoring is Sleepiness/Drowsiness detection in the normal life environment for patients with Excessive Daytime Sleepiness. As mentioned, excessive daytime sleepiness is the main symptom in OSA (and other less frequent sleep disorders) that affects patients' daily life. It is critical to evaluate sleepiness and drowsiness beyond the initiation of the treatment. Currently excessive sleepiness can only be objectively quantified in a sleep lab environment by using specific tests such as MSLT, OSLER, (see 4.2). Physiological data that are continuously transmitted from remotely located patients to a Contact Center is the new option and feedback can be given to the patient. There should be a standard protocol that defines the timing of the baseline measurement, treatment initiation, and regular follow-up assessments.

Tables 8 and 9 present the superset of outcome variables assessment instruments that can be used in clinical practice in order to evaluate insomnia and obstructive sleep apnea treatment [111]. Clinicians, after a thorough clinical interview, physical examination and psychological evaluation, will decide which of these variables and assessment instruments are appropriate in each individual patient case.

In the following months clinicians will define the detailed applications that will be developed in SP3. These tables could be used as a guide for the definition of the assessment variables and instruments that will be required for these applications.

Treatment Variables	Assessment instruments currently used
Sleep/wake behavior	Sleep Diary Actigraphy
Sleep stages	Polysomnography (In a few cases only)
Insomnia Symptoms	Insomnia severity index Pittsburgh sleep quality index Insomnia Athens Scale
Daytime Functioning	Fatigue severity scale
Fatigue	Multidimensional fatigue inventory
Performance	Reaction time (Simple/choice reaction time; continuous performance test) Attention (digit span; divided attention test) Coordination (digit symbol substitution; finger tapping) Auditory/visual vigilance Memory (word list, figures)
Psychological Symptoms	Beck depression inventory Beck anxiety inventory State-trait anxiety inventory Profile of mood states
Quality of Life (QOL)	SF-36 Sickness impact profile WHO QOL
Clinical utility	Treatment satisfactory/preference
Cost/Effectiveness	Health care utilization
Global assessment	Clinical global impression scale
Process outcome measures	Beliefs and attitudes about sleep scale Insomnia symptom questionnaire Sleep disturbance questionnaire Pre-sleep arousal scale

Table 8: Outcome variables for insomnia evaluation

Treatment Variables	Assessment parameters currently used
Sleep/wake behavior	Actigraphy Osler Test
Sleep stages	Polysomnography (PSG)
Apnea Evaluation Parameters	Apnea-hypopnea index (AHI) Arousals Desaturation Index Mean and minimum Saturation
Cardiovascular Evaluation parameters	ECG Heart Rate Blood pressure (optional)
OSA Symptoms	Loud irregular snoring Disrupted sleep Nocturnal gasping and choking Witnessed apnea Daytime sleepiness and fatigue Crowded posterior airway
Daytime Functioning	Epworth sleepiness scale Sleep disorders questionnaire Stanford sleepiness scale Beck depression inventory (BDI) MSLT (with EEG)
Fatigue	Multidimensional fatigue inventory Cognitive Tests (either questionnaires or computerized test)
Performance	Reaction time (Simple/choice reaction time) Attention (digit span; divided attention test) Coordination (digit symbol substitution; finger tapping) Auditory/visual vigilance Memory (word list, figures)
Quality of Life (QOL)	Body mass index (BMI) SF-36 Sickness impact profile WHO QOL
Clinical utility	Treatment satisfactory/preference
Cost/Effectiveness	Health care utilization
Global assessment	Clinical global impression scale
Process outcome measures	Beliefs and attitudes about sleep scale Sleepiness symptom questionnaire Sleep disturbance questionnaire Pre-sleep arousal scale

Table 9: Outcome variables for Obstructive Sleep Apnoea evaluation.

The following table presents the current status in assessing treatment variables for OSA and insomnia and innovations that can be achieved in SENSATION.

Treatment variables	Local Monitoring Current Status	Distant Monitoring Current Status	Innovation that can be achieved in SENSATION
PSG (OSA and very rarely for insomnia)	1. Long waiting lists in sleep labs 2. Very expensive exam 3. Not many sleep centers especially in small cities 4. Patients have to spend a whole night at a hospital 5. Not comfortable medical exam	1. Big variety of portable devices exist, however more systematic validation studies are required. 2.Guidelines and policies are still not promoting the use such devices 4. Most reliable devices are not fully portable Specialized personnel needed	1. Development of reliable, dry and stable EEG sensors 2. Development of fully portable, self-attached devices 3. Validation studies compared to Sleep Lab PSG 4. Development of more sensitive sensors for Oxygen Saturation 5. Development of more efficient, automated artifact rejection algorithms 6. Development of more advanced algorithms for sleep staging evaluation based on Peripheral Arterial Tone 7. Development of microchips that allow HRV and spectral estimation of EEG available in the microdevice.
Actigraphy (OSA and Insomnia)	Almost all sleep lab devices provide actigraphy data	Most of the portable devices provide actigraphy data	Wireless data downloading
Sleepiness Assessment from Behavioural Data (OSA and Insomnia)	**Osler Test** 1. High simplicity 2. Inexpensive medical test 3. Does not require the presence of a trained technician 4. Available only in Sleep Lab environment	Not available	Development of more efficient behavioral tests based on eyelid closure and blink speed
Sleepiness Assessment through Physiological Measurements (OSA and Insomnia)	**MSLT, MWT** 1. Available only in Sleep Lab environment 2. Time consuming exam (MSLT) because is administered four times throughout the day at two-hour intervals	Not available	Distant Physiological monitoring measuring sleepiness Wireless signal acquisition Development of camera-based micro sensors for EOG and motility parameters should also be useful
Sleep Diary (Insomnia)	1. Paper based sleep diaries are used 2. Not computerized	Not available	PDA (hand held devices) devices should be used for the questionnaires and diaries

Table 10: Current status in assessment of treatment variables and possible innovation that can be achieved.

5.3. Definition of functions and processes of distance monitoring

Currently, very few of the portable devices are really portable in the sense that they are self-applicable by the user. For a measurement equivalent to PSG, there is a maximum of 18 channels that have to be attached to the patients' body. For an in-home assessment study, patients visit the clinic, where a specialized technician (or physician) connects these sensors to their body. Then, patient goes home. After a one night's sleep, where all data has been recorded in a memory disc, patient goes back to the clinic with this memory disc. An alternative could be to have the technician sent to patient's home but that increases significantly the cost of the home study. In addition, during in-home studies, very often cables get damaged and the devices as well. Devices are rather expensive, and medical centers and clinics cannot risk having to buy frequently new devices.

Since a patient has been diagnosed to suffer from a sleep disorder, specific treatment should be prescribed by his/her clinician. We assume that in most sleep disorders a follow-up treatment is necessary. In such clinical cases, a sequence of sleep laboratory studies, such as PSG and MSLT, are useful for treatment effectiveness estimation. Treatment procedures are either continuous positive airway pressure (CPAP) for the case of obstructive sleep apnea or drug therapy that can affect the sleep/wake cycle. In addition, treatment follow-up acceptance issues such as CPAP treatment acceptance and compliance should also be considered.

Specific clinical cases in which treatment follow-up, through a telemedicine system, is necessary or would be beneficial for a patient were discussed in the first focus group, however more detailed scenarios are required.

In such clinical cases, the medical doctor is prescribing the use of the SENSATION equipment, and training them on how to use it. Patient goes home and is ready to use the equipment, while it would be desirable to have available videos and multimedia material for the patients, in order to achieve the best possible educational and use quality. Devices should be self attached with dry electrodes that enable recording of at least one EEG could be useful for brain dynamics study during all day sleepiness/drowsiness. Modern devices and techniques with the capability to record many signals in high resolution and to transfer signals to remote locations open new scope for SENSATION.

6. Conclusions

Portable systems for in-home assessment of sleep disorders described in the literature have been developed and evaluated primarily for OSA applications. Literature search has shown that the utility of Type III and Type IV devices for in home assessment of breath related measurements seems to be not so well established. Additional high quality studies are required to clarify the performance of portable monitors in the unattended setting. Therefore, in SENSATION particular emphasis should be placed in the design and implementation of high quality medical trials that would provide evidence specific to the clinical investigations, which can be performed with the developed equipment. The developed system has to be validated in an unattended setting and compared against standard in-lab procedures (PSG for the case of Obstructive Sleep Apnea) using reliable statistical methods.

Development of fully portable self-attached devices that enable sleep full EEG recording is in a preliminary stage. Two devices were found available in the market. The only device that was documented in the literature is Quisi [79]. However, the first validation study performed with it, showed that the resulted hypnogram is not reliable. In such devices, availability of EEG, EOG and EMG raw data should be a requirement. Furthermore, more advanced algorithms for sleep staging evaluation should be developed. Experts, during interview discussions and the focus group meeting, have agreed that one EEG, one EOG, and one EMG raw data signals should be available in the developed system.

As already stated above, the PAT signal can highly contribute to sleep staging assessment when combined with pulse rate, oxygen saturation, and actigraphy. All four measurements can be easily recorded in a portable device. This should be considered during the development of the SENSATION system.

To summarize, the current status of distance monitoring in sleep disorders is limited to methods for in-home assessment of breathing related sleep disorders. Even in these scenaria, no effort has been reported in the literature to integrate these devices into a telemedicine system. In SENSATION the developed sensors will be integrated in a telemedicine system that will allow clinicians to monitor patients with sleep disorders anytime-anywhere. It should be highlighted, however, that such a system

will become useful only if its utility in the setting of intended use is clearly understood and only if it is used according to clinician's discretion.

Medical applications will focus both on sleep and sleepiness/drowsiness monitoring. Clinicians agree that SENSATION system should be applied in the diagnosis of patients with insomnia, and/or hypersomnia complaints. Potential sleep disorders that are proposed to be investigated in SENSATION are Insomnia and Obstructive Sleep Apnea. Preliminary list of requirements appears in Tables 11-15. The detailed user requirements and scenarios for these target groups will be specified between project month 6 and 12, through interviews and focus group meetings and will be reported in D3.1.2.

Task	Requirement	Resulted from
System Functionality	The developed sensors have to be integrated in a telemedicine system that will allow long term follow up of patients with sleep disorders anytime-anywhere. A "contact center" will be the heart this system.	Interviews, focus group
Patient Training	Multi media material should be available for patient training with the Sensation equipment & procedures	Focus Group
System Evaluation	The developed system has to be validated through medical trials in an unattended setting and compared against standard in-lab procedures	Literature Search
	The Sensation system has to be evaluated during the clinical pilots using reliable statistical methods (including Pearson correlation coefficient, interclass correlation coefficient, the approach of Bland and Altman of mean differences and limits of agreement, and sensitivity / specificity / likelihood ratios).	Literature Search
	The following outcome variables can be used for evaluation of the Sensation system for each target group: • Sleep/Wake parameters • Symptoms • Daytime Functioning, Fatigue & Performance • Psychological Symptoms • Quality of Life (QOL) • Clinical utility • Cost/Effectiveness • Global assessment	Literature Search
	A list of guidelines should be generated that identify criteria for indications specific to the clinical studies that can be performed with the developed equipment.	Literature search

Table 11: Preliminary list of overall system requirements for the SENSATION SP3 System.

Task	Requirement	Resulted from
Standards	Classification as well diagnosis criteria will be based on ICSD.	Literature Search, Interviews, focus group
	Golden standard for evaluating in-home assessment of sleep against is in lab assessment through PSG	Literature Search, interviews
	Standard (test) assessment of sleepiness in lab environment is MSLT	Literature Search, interviews
	Proposed questionnaires for subjective measurement of sleepiness are ESS and KSS	Literature Search, interviews

Table 12: Preliminary list of standards proposed for the SENSATION SP3 System.

Task	Requirement	Resulted from
Monitoring of Respiration	Airflow CPAP pressure Respiratory effort Snoring sound Oxygen Saturation	Literature Search
Monitoring of Cardiovascular vital signs	ECG Heart Rate Peripheral Arterial Tone	Literature Search
Monitoring of movement and behavioral measures	Body position Acceleration Can be done through actigraphy	Literature Search
Sleep staging evaluation	More advanced algorithms for sleep staging evaluation based on Peripheral Arterial Tone signal should be developed	Interviews, Literature Search
	At least one EEG for sleep, one EOG, one ECG, one EMG raw data signals are required	Focus Group & Interview
Combinational measurements	Combination of spectral EEG and heart rate variability (HRV) since HRV is perhaps today the best tested way to measure changes in the ANS tone. Thus, from the SP2 people it is desirable that spectrum estimation would be available on	Focus Group

	the microdevice	
Monitoring of sleepiness/drowsiness	*See table 15*	

Table 13: Preliminary list of requirements for OSA diagnosis & follow-up.

Task	Requirement	Resulted from
Sleep staging evaluation	More advanced algorithms for sleep staging evaluation based on Peripheral Arterial Tone signal should be developed	Interviews, Literature Search
	At least one EEG for sleep, one EOG, one ECG, one EMG raw data signals are required	Focus Group & Interview
Monitoring of Subjective measures	Sleep diaries and self report questionnaires can be provided through hand held devices (PDA)	Literature Search, Focus Group

Table 14: Preliminary list of requirements for Insomnia treatment follow up.

Task	Requirement	Resulted from
Monitoring of sleepiness/drowsiness	Eye blink movement, 2EEGs, 1 EOG	Focus Group
	Car built in sensors so people to track the movements of steering wheels	Focus Group
	Combination is needed between the outputs of all the above mentioned measurements Analysis must be done on real time basis and an immediate correlation of changes is needed	Focus Group
	Alpha band topographic changes (frequency domain) could be a factor that could be linked with the drowsiness, but is not evidenced yet	Focus Group, Literature Search

Table 15: Preliminary list of requirements for sleepiness/drowsiness monitoring.

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APPENDIX I

Outline of Interviews to Clinicians (sent to clinicians, prior to the interviews)

INTRODUCTION

The aim of this first round of interviews is to receive clinician feedback based on their experience with portable devices and monitoring procedures (in non laboratory settings) for patients with sleep disorders. This information will result to the presentation of current ambulatory applications (non-laboratory) for sleep disorders. Their advantages and disadvantages will be reported. It will also facilitate the selection of clinical target groups to be studied in our project.

We will start with 5 Semi-structured phone interviews to clinicians participating in SP3. The current document presents an outline for the interviews although these questions are only a guide. Unanticipated issues that may arise could also be discussed. Each interview is expected to last about 30 minutes.

Interview Outline

Name:

Specialty:

Clinic:

Part A. General information

1. Do you agree to use the international classification of sleep disorders ICSD 1990 (see APPENDIX III) as a basis when referring to sleep disorders? (Dr Penzel had recommended another classification but unfortunately I could not find such a detailed list on that)

2. Which of these disorders (ICSD 1990) do you consider the areas of your expertise?

3. Which of these disorders (ICSD 1990) are most often treated at your clinic?

4. What is the cost (please give a range in euros) for an in-lab study at your clinic? (The annex states that the average cost is 390 euros per study, is this in accordance with the situation in your clinic?)

5. What is the cost (please give a range in euros) for an ambulatory study? (the annex states that the average cost is 120 euros per study, is this in accordance with the situation in your clinic?)

6. Do you have information on the prevalence rate in your country or Europe, for any of these sleep disorders (particularly for insomnia, sleep apnea, restless legs syndrome, and narcolepsy? If not, can you suggest where we should look for such data?

7. For which sleep disorders is diagnosis (or treatment) currently feasible through an ambulatory study? (in non-lab environment) Based on our literature

findings so far, all devices and such methods refer to the diagnosis of sleep apnea. Is that the case?

8. Which of these sleep disorders (ICSD 1990) are the main causes of: excessive day sleepiness, excessive fatigue, drowsiness, stress, inattention and other daytime symptoms? Is there evidence on that?

9. To your knowledge, are there any applications enabling the "monitoring" of excessive day sleepiness, excessive fatigue, drowsiness?

10. Criteria for selecting sleep disorders for which we could develop ambulatory monitoring applications in the context of this project:
    - High prevalence of this condition
    - Currently high cost in the diagnosis and treatment of this condition, and need to develop more cost-effective methods
    - Expertise in these disorders from SP3 clinical partners
    - Sleep disorders that are the main causes of excessive day sleepiness, excessive fatigue, drowsiness, stress, inattention and other daytime symptoms.
    - Availability of sensors that would enable ambulatory monitoring of this condition (this information is not currently available)

11. Which other criteria do you think are important and should influence the selection of sleep disorders for our project?

Part B. In this part you are requested to provide information for any portable device and procedure you are familiar with, for ambulatory monitoring of sleep disorders.

For each device, please answer the following questions:

1. What is the Device name?

2. What sleep disorder application is it used for? (Specify if it is used for diagnosis and/or treatment)

3. What parameter(s) is (are) monitored (airflow, oxygen levels in the blood, body position, breathing motion, heart rate, snoring noise, EEG, etc)?

4. Is the information you receive from this device satisfactory for the purpose you are using it for? What additional information/parameters would you wish to have?

5. Please list any references on this device (URL, article, etc)

6. You are familiar with this device because:
    - you use it routinely at your clinic
    - you have used it in research
    - other, please specify

7. If your answer in 5 is (a) then, briefly describe the procedure that is followed (what type of patients receive it, for how long, protocol of use)

8. If your answer in 5 is (a) then, are patients satisfied with the usage of this procedure and device?

9. If your answer in 5 is (a) how, in your opinion, could this device/procedure be improved? (Which additional features would it need)

10. If your answer in 5 is (b) then what are your expectations of this method?

11. What is your personal opinion on this device?

12. What are the advantages?

13. What are the disadvantages?

14. Please, answer this question only if the devices listed below are different from the one you described above.

15. The devices mentioned in the literature are the following:
    - Watch_PAT100
    - Embletta
    - NovaSom QSG

    Have you used any of these devices? If yes what were the main advantages and what the disadvantages?

16. Through our literature search, ambulatory methods in non-laboratory environments have been found only for sleep apnea, although, insomnia has a higher prevalence. Is this the case? If so, what are the limitations that do not allow other sleep disorders to be diagnosed through portable devices?

17. Are you familiar with any other approaches for in-home assessment of sleep disturbances and therapeutic effectiveness? If yes, please specify and list references if possible.

APPENDIX II

Synopsis of Interviews

Interview 1

Thomas Penzel (physiologist)

The international classification of sleep disorders, ICSD 1990, will be used as a reference. Although a revised classification has been ICSD-2 is currently available, it has not been yet evaluated, therefore the ICSD1990 will be used. Dr Penzel has provided the ICSD-2 proposed classification that is included in APPENDIX III.

The area of expertise of Dr Penzel is Dyssomnias and specifically intrinsic sleep disorders.

Sleep disorders management in the Philips Clinic, University of Marburg

The most commonly treated patients in the Philips Clinic, University of Marburg are:

- Obstructive sleep apnea syndrome
- Central sleep apnea syndrome
- Periodic limb movement disorder
- Psychophysiological insomnia
- Sleep state misperception
- Central alveolar hypoventilation syndrome

Cost and current sleep disorder management in Germany

The cost for a three-night lab exam is about 1000 Euros.

The cost of an ambulatory exam is estimated to be 150 euros, however, the re-imbursement is only 30 Euros. This limited amount automatically restricts the physicians to the use of portable devices with 4, maximum, number of channels.

The prevalence of insomnia is 10-20% in the population.

The prevalence of Sleep apnea is 6%.

However, re-imbursement for ambulatory diagnosis is offered only for sleep apnea diagnosis. For insomnia and periodic leg movement no ambulatory diagnostic

procedure has been yet established, therefore no re- imbursement is given. The main reason for that is that the diagnosis of these two disorders, very infrequently requires a sleep-lab investigation that could be replaced with an ambulatory diagnostic procedure. Physical exam and interview with the physician are the standard diagnostic procedures. Specifically, for the periodic leg movement disorder insomnia, 30% of the patients would need a sleep lab investigation while for insomnia patients this drops to 1%.

It has been established by research that sleep apnea is the main cause of excessive day sleepiness and drowsiness (Cohrane Collaboration).

Several reports state the connection between such daytime symptoms and other sleep disorders such as insomnia and periodic leg movement; however no evidence is published yet.

For sleep apnea ambulatory monitoring, 30% of the patients are clearly diagnosed, 30% are ruled out and for the 30% results are unclear and PSG at sleep lab has to be done.

In order to re-imburse treatment, sleep lab test has to be done, so the first 30% has to be retested in sleep lab.

Daytime sleepiness and performance are currently measured at sleep laboratories.

The only established test is the Multiple Sleep Latency test (MSLT). This is currently used at the specific clinic for professional drivers who need to get their professional license. In this test we take in 2 hours distances.

Other tests are:

- Reaction time test
- Vigilance test
- Sleepiness scales
- PVT
- Osler test
- Popylography (for daytime test)

For the SIESTA project, FourChoice reaction time test:

Sitting in front of Computer Monitor for 60-90 minutes.

4 symbols appear and disappear slowly (every 20-40 seconds) and user has to drive one of 4 nobs in order to bring back the symbol that disappeared.

The test is very long and not very reliable.

Interview 2

Luc Staner (psychiatrist)

The ICSD 1990 classification listed in the end of the interview outline report was incomplete and Dr Staner provided the complete document to AUTH.

ICSD is primarily used for research by sleep specialists, neurologists.

However, as approximately 50 % of the physicians working with sleep disorders belong to other specialties such as pneumonologists, the ICD-10 coding should be also proposed, since it is simpler and familiar to all physicians. DSM4 is another classification used primarily by psychiatric specialists.

During the first focus group meeting, it has to be decided which classification will be used in SENSATION, SP3.

At the Sleep Research center the majority of patients belong to the following groups:

A8 Obstructive sleep apnea syndrome

A1 Psychophysiological insomnia

A3 Idiopathic insomnia

A11 Periodic limb movement disorder

A12 Restless legs syndrome

B10 Hypnotic-dependent sleep disorder

C2 Shift work sleep disorder

C5 Advanced sleep phase syndrome

Sleep walking

Also patients with neurological disorders (epilepsy and Parkinson)

Cost and current sleep disorder management in France

The cost of a PSG exam at the lab is 136 euros per night, meaning 408 Euros for a three day exam. At the public hospitals in France, hospitalization is charged extra to this amount. At the "liberal" private centers, there is no extra charge for hospitalization. For an in-home exam the charge is 80 euros.

There is no official guideline in France, defining in which situations a PSG at the lab should be performed or at home through a portable device. It is up to the physician to decide, and then the prescribed exam is reimbursed.

A very strong campaign to reduce accidents caused by sleepiness is currently going on in France. It is of particular usefulness to develop the technology and introduce procedures that would enable monitoring sleepiness while driving.

With regards to the use of portable devices for in-home assessment of sleep disorders, in very few special cases in-home assessment is preferred. There are two main reasons for that:

No portable device so far provides valid EEG measurements. In order to "record" sleep the following signals are needed:

4 EEGs (one could be enough)

2 EOGs

2 EMGs (one could be enough)

Only one portable device allows so far for EEG recording, this is the Quisi device that synthesizes from 3 channels (EEG, EOG, muscle tone) an hypnogram.

As a way to measure day sleepiness, the multiple sleep latency test and the Osler test are used.

Interview 3

Lambrini Soufleri (neurologist)

Dr Soufleri works primarily with sleep apnea patients. The standard procedure for diagnosis is done based on PSG. She has used several portable devices for in-home assessment of sleep apnea but they are used only as an initial screening procedure for patients who are suspected to have sleep apnea, and more specifically to rule out sleep apnea. She has been involved in validation studies for the device Watch_Pat100 and she has been satisfied with its use.

Dr Soufleri provided valuable information on the use of PAT measurement in combination with pulse rate, oxygen saturation, and actigraphy for the detection of respiratory events and arousals from sleep. More specifically, PAT respiratory disorders index and PAT arousals index have been proposed for abnormal breathing events evaluation the standard clinical procedures that are currently being followed when taking PSG measurements.

For other type of diagnosis and treatment, in-lab PSG is only used. As measurement for sleepiness the ESS, Epworth Sleepiness Scale is used.

No official guidelines exist in Greece about the use of portable devices. This definitely constitutes a problem since, their use depend on the degree of training and expertise of the referring physician.

Interview 4

Chrysoula Kourtidou-Papadeli (pneumonologist)

The ICD-10 coding should be proposed, since it is simpler in comparison with the ICSD 1990 and familiar to all physicians, especially the pneumonologists.

The area of expertise of Dr. Kourtidou-Papadeli is Obstructive Sleep Apnea. The most commonly treated patients in the IASI Clinic in Thessaloniki are the obstructive sleep apnea syndrome, and the central sleep apnea syndrome.

The cost for a sleep lab exam consisted of three sessions is about 350 Euros. The cost of an ambulatory exam is estimated to be 100 euros.

Sleep apnea is the main cause of excessive day sleepiness and drowsiness.

For sleep apnea ambulatory monitoring, 20% of the patients are clearly diagnosed, 30% are ruled out and for the 40% results are unclear and PSG at sleep lab has to be done.

Dr. Kourtidou-Papadeli suggests Type 3 ambulatory devices for the diagnosis of Obstructive Sleep Apnea in an unattended setting.

No official guidelines exist in Greece about the use of portable devices.

APPENDIX III

ICSD 1990 International Classification of Sleep Disorders

The classification outline is presented below. In the current list the diagnostic criteria for each disorder are not listed.

1. Dyssomnias (disorders of initiating and maintaining sleep and disorders of excessive sleepiness)
2. Parasonmias (disorders that primarily do not cause a complaint of insomnia or excessive sleepiness)
3. Sleep Disorders Associated with Medical/Psychiatric Disorders
4. Proposed sleep disorders

1. Dyssomnias (disorders of initiating and maintaining sleep and disorders of excessive sleepiness)

A. Intrinsic sleep disorders

1. Psychophysiological insomnia
2. Sleep state misperception
3. Idiopathic insomnia
4. Narcolepsy
5. Recurrent hypersomnia
6. Idiopathic hypersomnia
7. Posttraumatic hypersomnia
8. Obstructive sleep apnea syndrome
9. Central sleep apnea syndrome
10. Central alveolar hypoventilation syndrome
11. Periodic limb movement disorder
12. Restless legs syndrome
13. Intrinsic sleep disorder NOS

B. Extrinsic sleep disorders

1. Adjustment sleep disorder
2. Insufficient sleep syndrome
3. Limit-setting sleep disorder
4. Sleep-onset association disorder
5. Food allergy insomnia
6. Nocturnal eating (drinking) syndrome
7. Hypnotic-dependent sleep disorder
8. Stimulant-dependent sleep disorder
9. Alcohol-dependent sleep disorder
10. Toxin-induced sleep disorder
11. Extrinsic sleep disorder NOS

C. Circadian rhythm sleep disorders

1. Time zone change (jet lag) syndrome
2. Shift work sleep disorder
3. Irregular sleep-wake pattern
4. Delayed sleep phase syndrome
5. Advanced sleep phase syndrome
6. Non-24 hour sleep-wake disorder
7. Circadian rhythm sleep disorder NOS

2. Parasonmias (disorders that primarily do not cause a complaint of insomnia or excessive sleepiness)

A. Arousal disorders

1. Confusional arousals
2. Sleepwalking
3. Sleep terrors

B. Sleep-wake transition disorders

1. Rhythmic movement disorder
2. Sleep starts

3. Sleep talking

4. Nocturnal leg cramps

C. Parasomnias usually associated with REM sleep

1. Nightmares

2. Sleep paralysis

3. Impaired sleep-related penile erections

4. Sleep-related painful erections

5. REM sleep-related sinus arrest

6. REM sleep behavior disorder

D. Other Parasomnias

1. Sleep bruxism

2. Sleep enuresis

3. Sleep-related abnormal swallowing syndrome

4. Nocturnal paroxysmal dystonial

5. Sudden unexplained nocturnal death syndrome

6. Primary snoring

7. Infant sleep apnea

8. Congenital central hypoventilation syndrome

9. Sudden infant death syndrome

10. Benign neonatal sleep myoclonus

11. Other Parasomnia NOS

4. Proposed sleep disorders

These are the disorders for which insufficient information is available to confirm their acceptance as definitive sleep disorders.

1. Short sleeper

2. Long sleeper

3. Subwakefulness syndrome

4. Fragmentary Myoclonus

5. Sleep hyperhidrosis

6. Menstruation-associated sleep disorderly

7. Pregnancy-associated sleep disorder

8. Terrifying hypnagogic hallucinations
9. Sleep-related neurogenic tachypnea
10. Sleep-related laryngospasm
11. Sleep choking syndrome

ICSD-2 Proposed International Classification of Sleep Disorders

ICSD 2
Proposed Sleep Disorders Categories and Individual Sleep Disorders
(As of Jan 18, 2004)

Proposed ICD-9-CM numbers listed first, proposed ICD-10-CM numbers listed second

Insomnia

30742 F5101 Psychophysiological Insomnia
30742 F5102 Paradoxical Insomnia
30741 F5103 Adjustment Sleep Disorder (Acute Insomnia)
30741 F5104 Inadequate Sleep Hygiene
78052 G4701 Idiopathic Insomnia
78052 G4702 Fatal Familial Insomnia
30742 F5105 Behavioral Insomnia of Childhood
Limit-setting Sleep Disorder
Sleep-onset Association Disorder
78052 G4709 Other Insomnia due to a physiological condition (other organic insomnia)
29189 F10-19 Other Insomnia due to a substance
9952 T36-50
30742 F5109 Other Insomnia not due to a substance or physiologic condition (other psychiatric/behavioral insomnia)

Sleep Related Breathing Disorder

Central Sleep Apnea Syndromes:
78051 G4731 Primary Central Sleep Apnea
78057 G4739 Other Central Sleep Apnea, including
Cheyne Stokes Breathing Pattern
High Altitude Periodic Breathing
77081 P283 Primary Sleep Apnea of Newborn

Obstructive Sleep Apnea Syndromes:
78053 G4732 Obstructive Sleep Apnea, Adult
78053 G4732 Obstructive Sleep Apnea, Pediatric
78053 G4730 Other Obstructive Sleep Apnea Syndrome
780.53 G4733 Mixed Sleep Apnea Syndrome

78057 G4739 Other Sleep Related Breathing Disorder due to a physiological condition
9952 T36-50 Other Sleep Related Breathing Disorder due to a substance

PS: “Obstructive Sleep Apnea” includes all forms of sleep related obstructive breathing including Apneas, Hypopneas, UARS, etc.

Hypersomnia not due to a sleep related breathing disorder

Narcolepsy
3471 G4741 Narcolepsy with Cataplexy
3472 G4742 Narcolepsy Without Cataplexy
3477 G4749 Other Narcolepsy

Hypersomnia not due to a sleep related breathing disorder or narcolepsy
78054 G4711 Recurrent Hypersomnia
78054 G4712 Idiopathic Hypersomnia with long sleep time
78054 G4713 Idiopathic Hypersomnia without short sleep time
30744 F5111 Insufficient Sleep Syndrome

Other Hypersomnia
78054 G4719 Other Hypersomnia due to a physiological condition
29189 F10-19 Other Hypersomnia due to a substance
9952 T36-50
30744 F5119 Other hypersomnia not due to a substance or physiologic condition (other psychiatric or behavioral hypersomnia

Circadian Rhythm Sleep Disorder

Primary Circadian Rhythm Sleep Disorder
78055 G4721 primary, delayed sleep phase type
78055 G4722 primary, advanced sleep phase type
78055 G4723 primary, irregular sleep-wake type
78055 G4724 primary, free running type
78055 G4720 primary, unspecified

Behaviorally Induced Circadian Sleep Disorders
30745 F5121 not due a substance or known physiological condition, jet lag type
30745 F5122 not due to a substance or known physiological condition, shift-work type
30745 F5123 not due to a substance or known physiological cond., delayed sleep phase type
30745 F5124 not due to a substance or known physiological cond., advanced sleep phase type
30745 F5124 not due to a substance or known physiological cond., irregular sleep phase type
30745 F5120 not due to a substance or known physiological cond., unspecified type

Other Circadian Rhythm Sleep Disorders
78055 G4729 Other Circadian Rhythm Sleep disorder due to a physiological condition
29189 F10-19 Other Circadian Rhythm Sleep disorder due to a substance
9952 T36-50
30745 F5129 Other Circadian Rhythm Sleep Disorder not due to a substance or physiologic condition (other psychiatric or behavioral circadian rhythm sleep disorder)

Parasomnia

Disorders of Arousal (From Non-REM Sleep)
78056 G4751 Confusional Arousals
30746 F513 Sleepwalking Disorder
30746 F514 Sleep Terror Disorder

Parasomnias Usually Associated with REM Sleep
78056 G4752 REM Sleep Behavior Disorder, including
Parasomnia Overlap Disorder
Status Dissociatus
78056 G4753 Recurrent Isolated Sleep Paralysis
30747 F515 Nightmare Disorder

Other Parasomnias
30015 F449 Nocturnal Dissociative Disorder

78836 N3944 Nocturnal Enuresis
78056 G4759 Catathrenia (Nocturnal Groaning)
78056 G4759 Exploding Head Syndrome
78056 G4759 Sleep Related Eating Disorder

78056 G4759 Other Parasomnia due to a physiologic condition
29189 F10-19 Other Parasomnia due to a substance
9952 T36-50
30747 F5139 Other parasomnia not due to a substance or physiologic condition (Other psychiatric or behavioral parasomnia)

Sleep Related Movement Disorder
78058 G4761 Restless Legs Syndrome (including Sleep Related Growing Pains)
78058 G4762 Periodic Limb Movement Sleep Disorder
78058 G4765 Sleep Related Rhythmic Movement Disorder
78054 G4769 Other Sleep Related Movement Disorder due to a physiological condition
29189 F10-19 Other Sleep Related Movement Disorder due to a substance
9952 T36-50
30744 F5119 Other Sleep Related Movement Disorder not due to a substance or physiologic condition (other psychiatric/ behavioral sleep-related movem. d/o

Other Sleep Disorder
30749 F518 Environmental Sleep Disorder
78059 G478 REM Sleep Related Sinus Arrest
78050 G479 Sleep Disorder related to a physiologic condition, unspecified
29189 F10-19 Sleep Disorder related to substance use, unspecified
9952 T36-50
30740 F519 Sleep Disorder not due to a substance or physiologic condition, unspecified

Isolated Symptoms, apparently Normal Variants and Unresolved Issues
30749 R2981 Long Sleeper
30749 R2981 Short Sleeper
78609 R065 Snoring
30749 R2981 Sleeptalking
30749 R2981 Sleep Related Hallucinations
78101 R258 Sleep Starts, Hypnic Jerks
78101 R258 Benign Sleep Myoclonus of Infancy
78101 R258 Hypnagogic Foot Tremor
78101 R258 Propriospinal Myoclonus at Sleep Onset
78101 R258 Sleep and Exercise Related Dystonia

Appendix A: Other Organic Disorders frequently encountered in the Differential Diagnosis of Sleep Disorders.

Other Sleep Related Hypoventilation/Hypoxemic Syndromes:
78057 G4734 Sleep Related Non-obstructive Alveolar Hypoventilation, Idiopathic
78057 G4735 Congenital Central Alveolar Hypoventilation Syndrome

78057 G4739 Sleep Related Non-obstructive Alveolar Hypoventilation
78057 G4739 Sleep Related Hypoxemia (e.g. pulmonary parenchymal or vascular disease)

78058 G4763 Sleep-related Leg Cramps
78058 G4764 Sleep Related Bruxism

78059 G478 Sleep Related Epilepsy
78059 G478 Sleep Related Headaches
78059 G478 Sleep Related Gastroesophageal Reflux Disease
78059 G478 Sleep Related Coronary Artery Ischemia
78059 G478 Sleep Related Abnormal Swallowing
78059 G478 Sleep Related Choking
78059 G478 Sleep Related Laryngospasm

Appendix B: Other Psychiatric/Behavioral Disorders frequently encountered in the Differenti Diagnosis of Sleep Disorders

To be developed, will include depressive disorders, anxiety disorders, panic disorders, psychosis, e

Appendix C: Atypical Polysomnographic Findings (no codes)

Alpha Intrusions
Cyclic Alternating Pattern
Alternating Leg Muscle Activation during Sleep
Fragmentary Myoclonus

APPENDIX IV

SP3 Focus Group 1

Participants

Nicos Maglaveras

Stavroula Maglavera

Thomas Penzel

Georg Gruber

Grau

COAT

In the context of WP3.1, the user requirements for a telemedicine approach for patients with sleep disorders need to be defined. For this purpose a focus group is being organized during the Barcelona meeting. More specifically, the details for this focus group are:

Purpose:

- To describe a realistic clinical scenario of **sleep** monitoring through a telemedicine system
- To describe a realistic clinical scenario of **sleepiness/drowsiness** monitoring through a telemedicine system

Facilitator: Nicos Maglaveras

Participants: all SP3 clinicians who are participating in the Barcelona meeting (most of these clinicians are also participating in SP1 and SP2). We encourage clinicians participating in other SP's to be present, however the total number of participants should not exceed 8 persons.

Duration of the focus group meeting: 2 hours

Agenda:

- Purpose of the current focus group,
- Brief oral presentation of the concept of a distance monitoring system
- Brief oral presentation of the status of sleep disorders in distance monitoring

Nicos Maglaveras, (5-10 minutes)

Discussion of Question 1

>> of Question 2

Description of the sleep scenario

Discussion of Question 3

Description of the sleepiness/drowsiness scenario

List of questions that could lead to the scenarios description:

Question 1 (Sleep disorders diagnosis / distance monitoring of sleep)

We assume that a sleep recording portable device will be used at a home environment. Such devices currently allow for recording of respiratory and cardiovascular activity and body movement parameters. In the context of the current project, EEG, EMG and EOG could potentially also be recorded at a home environment.

We also assume that the recorded data can afterwards be sent (through telephone/ Internet/ wireless) to the sleep clinic where it can be reviewed by specialists. Clinician-patient communication could also be feasible through mobile technology (message through mobile, PDA etc).

It is not clear whether portable devices integrated in a telemedicine system will be helpful during sleep disorder diagnosis. In this case, the patient borrows a device from the clinic, uses it for a few sessions and then he/she returns it to the clinic where recorded data are retrieved.

What would be the benefit of a telemedicine approach for sleep disorders diagnosis?

Thomas: What we can monitor is EEG, EOG and EMG and general skeleton

How many sensors: 1 EEG for sleep, 1EOG, 1 ECG, 1 EMG for the legs forming an ensemble of information since a combination is needed

What about synchronization between the four type of sensors? This must be requested by SP2 since it is considered to be a must. It seems that ECG and especially the R wave is a serious candidate for the synchronization issue.

What type of patients

- Potential patients of Insomnia (people that complaint)
- Potential patient of Hypersomnia (people that complaint)

We are talking about complaints sine diagnosis has not been done yet, but people complaint and have symptoms of the disease.

Then we arrive to diagnosis. So we go with ICSD (International Classification of Sleep disorders). ICD9 is the one that is being used.

Scenario

Somebody is complaining of insomnia, snoring, hypersomnia, is overweight, has respiratoty problems, shortness of breath, is awake at nights, exerts involuntary movements of legs, and feels restless.

The scenario will cover symptomatic cases.

Then the citizen is consulting the physician and the medical doctor is prescribing the use of the SENSATION equipment, training them how to use (place it, use it, etc)

Patient goes at home at is ready to use the equipment, while it would be desirable to have available videos and MM material for the patients in order to achieve the best possible educational and use quality.

We must have a combination of spectral EEG and heart rate variability (HRV) since HRV is perhaps today the best tested way to measure changes in the ANS tone. Thus, from the SP2 people it is desirable that spectrum estimation would be available on the microdevice.

Question 2 (distance monitoring of sleep/ treatment follow-up)

Since a patient has been diagnosed with a sleep disorder, specific treatment should be prescribed by his clinician. We assume that in most sleep disorders a follow-up treatment is necessary. In such clinical cases, sequent sleep laboratory studies, such as PSG and MSLT, are useful for treatment effectiveness estimation. Treatment procedures are either continuous positive airway pressure (CPAP) for the case of obstructive sleep apnea or drug therapy that can affect the sleep/wake cycle. In addition, treatment follow-up acceptance issues such as CPAP treatment acceptance and compliance should also be considered.
We need to describe specific clinical cases in which treatment follow-up (CPAP or drug therapy) through a telemedicine system are necessary or would be beneficial for a patient.

Simple Questionnaire is enough for insomnia cases

For the rest of the patients a simple questionnaire will be used through a contact center and the doctor will decide when the patient needs specific monitoring

For narcolepsy etc we need a night of monitoring per month

Question 3 (distance monitoring of sleepiness/drowsiness)

Patients with sleep disorders present with a variety of complaints including excessive daytime sleepiness (EDS), uncomfortable sensation in the extremities, and daytime spells. Patients with EDS frequently doze, nap, or fall asleep in situations where they need or want to be fully awake and alert. Thus, sleepiness monitoring is of fundamental importance for patients and co-workers safety. Describe a realistic clinical scenario of **sleepiness** monitoring through a telemedicine system for a patient with sleep disorder. Moreover, physiological measurements that will be used for sleepiness/drowsiness estimation should also be defined.

We need eye link movement for the monitoring of sleepiness and drowsiness

Alpha band topographic changes (frequency domain) could be a factor that could be linked with the drowsiness, but is not evidenced yet.

PDA or other types of car built in sensors so people to track the movements of steering wheels

3 sensors= 2 EEG and 1 EOG

A combination is needed between the outputs of all the above-mentioned measurements

Analysis must be done on real time basis and an immediate correlation of changes is needed

The interSP committee said that that there are no minimum requirements and SENSATION will not aim to sell devices.