Impact of Insomnia on Health-Related Quality of Life

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Summary

With the increased interest in sleep disorders, the definition of insomnia has been refined and extended so that the aetiology of these disorders is considered in addition to their operational characteristics. The International Classification of Sleep Disorders is the most advanced nosology available. It encompasses, although it does not define, the concept that sleep may be disturbed either through disruption of the mechanisms that control sleep and wakefulness, or by factors external to those mechanisms. Formal measures of quality of life invariably include assessment of sleep or the consequences of disturbed sleep, such as fatigue. Generally, when these assessments are used, sleep has been disturbed by external factors, rather than by disruption of the mechanisms that control sleep.

Occasional insomnia does not necessarily need medical treatment, but it may nevertheless cost national economies significant sums through absenteeism and sleep-related accidents. Profound, longer term insomnias may arise either because of failure of the mechanisms central to sleep (i.e. as sleep disorders) or as a consequence of medical disorders (i.e. as disordered sleep). These insomnias should be treated, because the former may lead to the development of costlier and more intransigent psychiatric disorders, whereas the latter should be treated for compassionate reasons, within the framework of palliative medicine. Insomnia as a sleep disorder can require either psychological or pharmacological treatment, depending on the diagnosis, whereas insomnia as a symptom may require treatment with newer hypnotics, e.g. zopiclone.

Quality of life is a universally recognised term, although its origin is unknown and it is difficult to define.[1] Initial research work in the area of quality of life involved evaluation of cancer therapies. It was recognised that quality-of-life was as important as, or even more important than, simply the number of patients surviving over a given period of time.[2] Since then, quality-of-life assessment has been extended to chronic, non–life-threatening conditions.

One generally accepted definition of quality of life is 'the functional impact of an illness and its consequent therapy upon the patient, as perceived by the patient'.[3] It includes the following domains: physical (the ability to conduct activities of daily living), psychological (often considered only in terms of emotional problems) and social (interactions with family, friends and community). Insomnia affects all 3 of these domains: it impairs the ability to work both accurately and intensively, it causes emotional upset, both directly and indirectly, and it is associated with irritability and hostility.

Before its impact on health-related quality of

life can be evaluated, it is also necessary to define insomnia. In recent years, it has become increasingly clear that insomnia is not simply a problem with falling or remaining asleep, even though it can be defined in those terms. It can be either a sleep disorder (see section 1.1.1), or it can arise from a multitude of clinical (e.g. see section 2.3) or subclinical sources (e.g. noise, temperature, etc., see section 2.2).

Insomnia is associated with poor job performance,[4] diminished general physical and mental health,[5] and psychological disturbances.[6,7] It has been estimated to cost the US economy between $US92.5 and $US107.5 billion a year[8] through the effects of absenteeism and sleep-related accidents alone. However, even if the cost to society were zero, it would still be inappropriate to refuse treatment for patients distressed by their insomnia. For some insomnias, therapy based on palliative principles may be more appropriate than treatment based simply on pathology.

1. Insomnia

1.1 Sleep Disorders Classification

The International Classification of Sleep Disorders (ICSD), which was produced by the American Sleep Disorders Association together with the European Sleep Research Society, the Japanese Society of Sleep Research and the Latin American Sleep Society, provides a useful diagnostic framework.[9] Table I highlights the main categories associated with insomnias. It modifies the description of the main categories by further categorising the disorders as Sleep Disorders and Disordered Sleep. This distinction is made to promote the notion that sleep can be disordered by the failure of mechanisms central to sleep (sleep disorders) and that sleep can be disturbed by factors not associated with its control and expression (disordered sleep). The main point to be made in this context, however, is that insomnia is not simply a symptom. It has many causes, and it may also manifest itself in a variety of ways.

1.1.1 Sleep Disorder

It is only in recent years that psychophysiological insomnia, an intrinsic sleep disorder, has been recognised as a distinct diagnostic category; thus, prevalence figures are rare. However, in a recent survey of patients with insomnia who were referred to US sleep disorders centres, it was found that 12.5% were suffering from psychophysiological insomnia.[10] Persistent psychophysiological insomnia may be the result of learning poor sleep habits. In 1979, the American Sleep Disorders Centers nosology suggested that this type of insomnia was driven by 2 mutually reinforcing factors: 1) tension-anxiety that is chronic and somatised, leading not only to insomnia but also to tension headaches, backaches, palpitations, etc.; and 2) negative conditioning, consisting of internal (the fear of being unable to sleep) and external (the sleeping environment or bedtime rituals) conditioned reinforcers.[11]

The same study also revealed a high incidence (32% of referred patients) of previously undetected mood disorders that were associated with insomnia. In another study, 105 general practice attendees with chronic insomnia were evaluated for mental and personality disorders.[12] 50% were found to have additional diagnoses, affective disorders and substance abuse being the two most common. This study also noted that GPs were poor at recognising chronic insomnia and the high percentage of substance abusers among such patients.

1.1.2 Disordered Sleep

Sleep preceded by stressful events during the day has been found to be associated with decreased stage 4 sleep and increased spontaneous electrodermal activity.[13]

Prevalences of insomnia across countries appear to vary widely, as insomnia can be defined in different ways.[14] However, Janson et al.[14] recently used identical measurement techniques to compare a random population of 2202 individuals in Iceland, Sweden and Belgium and found that 1) there were no between-country differences in the time it took to fall asleep; and 2) the prevalence of disturbed sleep onset between countries ranged

Table I. Sleep disorders according to modified ICSD (parasomnias and proposed sleep disorders omitted). Sections in italics are proposed disordered sleep

Sleep disorder	Intrinsic sleep disorders	Psychophysiological insomnia
		Sleep state misperception
		Idiopathic insomnia
		Narcolepsy
		Recurrent hypersomnia
		Idiopathic hypersomnia
		Post-traumatic hypersomnia
		Obstructive sleep apnoea syndrome
		Central sleep apnoea syndrome
		Central alveolar hypoventilation syndrome
		Periodic limb movement disorder
		Restless legs syndrome
Dyssomnias	Extrinsic sleep disorders	*Inadequate sleep hygiene*
		Insufficient sleep syndrome
		Adjustment sleep
		Environmental sleep disorder
		Altitude insomnia
		Limit-setting sleep disorder
		Sleep-onset association disorder
		Food allergy insomnia
		Nocturnal eating (drinking) syndrome
		Hypnotic-dependent sleep disorder
		Stimulant-dependent sleep disorder
		Alcohol-dependent sleep disorder
		Toxin-induced sleep disorder
	Circadian rhythm sleep disorders	Time zone (jet lag) syndrome
		Shift work sleep disorder
		Irregular sleep-wake pattern
		Delayed sleep phase syndrome
		Advanced sleep phase syndrome
		Non–24-hour sleep-wake disorder
Disordered sleep	Associated with mental disorders	*Psychoses*
		Mood disorder
		Anxiety disorder
		Panic disorder
		Alcoholism
Sleep disorders associated with medical or psychiatric disorders	Associated with neurological disorders	*Cerebral degenerative disorders*
		Dementia
		Parkinsonism
		Fatal familial insomnia
		Sleep-related epilepsy
		Electrical status epilepticus of sleep
		Sleep-related headaches
	Associated with other medical disorders	*Sleeping sickness*
		Nocturnal cardiac ischaemia
		Chronic obstructive pulmonary disease
		Sleep-related asthma
		Sleep-related gastro-oesophageal reflux
		Peptic ulcer disease
		Fibrositis syndrome

Abbreviation: ICSD = International Classification of Sleep Disorders.

from 6 to 9%. Independent risk factors for disordered sleep included snoring, gastro-oesophageal reflux, smoking, age, and gender.

A cross-sectional survey administered via voice mail and telephone interview attempted to measure the prevalence of sleep problems in a working population and to examine their association with health problems, health-related quality-of-life measures, work-related problems, and medical expenditures.[15] 30% of respondents reported current sleep problems and were found to have poorer functioning and well-being, more work-related problems, and a greater likelihood of co-morbid physical and mental health conditions than the respondents with no sleep problems. There was also a trend towards higher medical expenditures in those with sleep problems.

Many patients do not complain about their insomnia. In a recent Spanish epidemiological study of 490 patients attending a primary care facility,[16] 62% had insomnia at the time of the survey but only 44% had sought medical advice for the problem.

A longitudinal study of 2512 patients attending general practitioners noted that diagnoses of insomnia made on the basis of simple labels such as sleep-onset insomnia, maintenance insomnia, or early morning awakening were not stable.[17] Only half the patients returning 4 months later remained in the same categories.

1.1.3 Sleep Disturbance Associated with Mental Disturbance

Insomnia is often associated with mental disturbance. Prolonged insomnia may herald or cause a mental disorder. Certainly, epidemiological data suggest that chronic insomnia is associated with an increased probability of developing profound mood disorders.[18] Laboratory data also reveal systematic changes in sleep architecture.[19] Sleep disruption and sleep deprivation in normal volunteers often result in disturbed mood, both in the young[20-22] and the elderly.[23,24] Jet lag can also cause mood state disturbance.[25-27] Furthermore, it is well established that increased anxiety and arousal,[28-32] and depression, have been found in volunteers reporting insomnia.

Early studies using the Minnesota Multiphasic Personality Inventory (MMPI) reported higher individual scores, as well as a greater number of elevated scores, in patients with insomnia compared with controls.[33] The most consistent elevations were for depression, hysteria, hypochondriasis and psychasthenia. However, the increasing precision in classifying insomnia has left many of these studies with arguably heterogeneous groups. This may explain the more recent finding that, of the patients with insomnia who have been classified according to the new nosologies, only those with psychiatric or psychophysiological disorders, and drug and alcohol users, were found to have elevated MMPI scores.[34]

2. Quality of Life

2.1 Introduction

Most formal measures of quality of life include either 1) direct sleep assessments, 2) sleep-related items (e.g. daytime fatigue), or 3) disorders that invariably include disordered sleep, such as depression. Table II provides some examples of quality-of-life scales that include items either directly or indirectly related to sleep; the list presented is not exhaustive, but it does include the major scales.

2.2 Health and Quality of Life

2.2.1 Age

Insomnia is common in the elderly population, and difficulty in initiating and maintaining sleep affects nearly half of all patients aged > 65 years. Nocturnal sleep time is decreased, frequent awakenings occur, and daytime napping is common. Multiple aetiologies for insomnia in the elderly have been described.[41]

In a recent epidemiological study of 9000 men and women aged ≥ 65 years, it was found that less than 20% of the participants did not have a sleep complaint.[42] Between 23 and 34% had symptoms of insomnia, and 7 to 15% rarely or never felt rested after waking up in the morning. Further analysis revealed an increasing number of respiratory symptoms, physical disabilities, depressive symp-

Table II. Quality-of-life measures

Quality-of-life measure	Sleep or depression-related items[a]	Reference
Linear analogue self-assessment	Difficulty with sleep	35
Manitoba Cancer Treatment and Research Foundation Functional Index: Cancer	*Most people experience some feeling of depression at times*	36
Nottingham Health Profile	I have tablets to help me sleep *(Things are getting me down)* (I'm tired all the time)	37
Sickness Impact Profile	I sleep or nap during the day	38
Profile of mood states	*Unable to concentrate; fatigued; energetic; exhausted*	39
Hospital Anxiety and Depression Scale	I still enjoy the things I used to enjoy	40

a   Depression-related items are italicised.

toms and increased use of nonprescription medications, as well as poorer self-perceived health in this group.

Phase-advance and increased daytime sleepiness occur in parallel with the deterioration of night-time sleep.[43,44] These may occur because of circadian changes (e.g. the rate of internal desynchronisation has been found to increase)[45] and, possibly, because of a return to poly-cycle sleep-wake patterns,[46] lack of environmental stimulation[47] and increased presence of sleep pathology.[48,49]

However, careful studies of sleep in the elderly show little correlation between age and poor sleep,[50-53] and disease and chronic illness may have a greater impact than age itself.[54] An epidemiological survey conducted in northern Sweden of all 10 216 members of the Swedish Pensioners' Association[55] showed that general ill health, cardiovascular diseases, different painful diseases and increased frequency of nocturnal voiding were all associated with poor sleep and increased treatment with hypnotics, which were used by 13.5% of the men and 22.3% of the women. Of the men, 7.9% of those aged < 70 years, 14.4% of those aged 70 to 80 years, and 21.8% of those aged ≥ 80 years were taking hypnotics. The corresponding frequencies among women were 15.0, 23.0 and 34.9%, respectively. Half of all men and women

treated with hypnotics in all age groups reported a good night's sleep.

2.2.2 Smoking, and Prescribed, Pharmacy and Consumer Drugs

Survey data from 3516 adults were collected as part of a longitudinal, epidemiological study of sleep-disordered breathing.[56] Among both males and females, smoking was associated with difficulty initiating sleep and difficulty waking up. Excessive daytime sleepiness was related to smoking only for females, while nightmares and disturbing dreams were related to smoking only among males. The authors suggest that sleep disturbance may be more common among smokers because of the stimulant effects of nicotine, nightly withdrawal, and an increased prevalence of sleep-disordered breathing compared with nonsmokers.

Another epidemiological survey of sleep disorders, which was conducted in the metropolitan area of Montreal, found that 5% of respondents used psychotropic drugs.[57] This use was often chronic, and it was more frequent among the elderly and women. These drugs were usually prescribed by a GP (72.9%). Psychotropic drug use was associated with females aged ≥ 55 years, the presence of physical illness, a medical consultation, dissatisfaction with sleep onset period and sleep quantity, sleep onset period greater than 15 minutes, and no or rare dreaming. Comparison of users with nonusers with sleeping difficulties

showed that users were more likely to be older, to have been formerly married, and to be experiencing regular night-time awakenings. Furthermore, when sleep satisfaction was measured, it did not appear that the quality of sleep was improved in those taking psychotropic drugs compared with nontreated individuals with insomnia.

Epidemiological studies invariably find that caffeine is associated with a high prevalence of insomnia.[58,59] The profound effects of caffeine on sleep are not always recognised, as its pharmacokinetics are complicated. The half-life of caffeine is between 3 and 5 hours, but its half-life in the brain can be tripled with increasing concentrations. In addition, many factors affect caffeine disposition: moderate exercise, polymorphism, pregnancy, liver disease and grapefruit juice.

2.2.3 Work

In industrialised countries, shift workers are currently estimated to constitute approximately 20% of the working population. Insomnia may be one of the major consequences of shift work. The relationship between shift work and sleep quality in a female population has recently been studied.[60] 469 nurses at 6 public hospitals in various French regions were interviewed in 1980, 1985 and 1990 about their working conditions and health. The results showed that at the beginning of the study in 1980 sleep disorders were more common in nurses on alternating schedules including night work; however, there was no association between shift work and sleep quality after that year. The absence of a relationship between time schedules and sleep in 1985 and 1990 may have arisen because nurses who could not adapt to shift work either left the profession or avoided those shifts. Sleep disorders predicted transfer from shift work to day work between 1980 and 1985, and sleep disorders decreased strongly after such transfer.

2.3 Illness and Quality of Life

The ICSD identifies a number of medical disorders that modify sleep (table I), but there are many more that affect quality of life. Rheumatoid arthritis, end-stage renal disease and multiple sclerosis are all associated with restless sleep and emotional distress, which could be improved with appropriate treatment.[61] Cancer, cardiovascular and gastrointestinal disorders, and AIDS are considered in more detail below.

2.3.1 Cancer

The UK Sickness Impact Profile was used to assess health-related quality of life in 212 cancer patients (average age 55 years; 143 women) compared with 105 age-sex matched controls (71 women).[62] The 4 main areas of impairment in the cancer patient group were sleep and rest, work, recreation and pastimes, and home management. Many patients had difficulty sleeping at night and tended to sleep during the day or rest for much of it. Most of the patients were unable to work or worked shorter hours, and a reduction in active leisure pursuits also lessened participation in social and community activities. Patients had particular problems in carrying out household chores and maintenance or repair work in the home. Most quality-of-life studies in oncology patients concentrate upon alterations in symptoms, but patient care would be improved if active management of sleep-wake behaviour was also undertaken.

A sample of 69 women with lung cancer described their symptom distress using the Symptom Distress Scale.[63] Most of the women (86%) had been diagnosed with primary or recurrent lung cancer within the previous 2 years, and 43% were currently receiving treatment. The most prevalent and distressing symptoms included insomnia, fatigue and frequent pain. 41% of the women with fatigue concurrently experienced frequent pain, and 31% had insomnia. Treatment was not a significant factor with regard to distress, which was strongly correlated with quality of life and functional status.

Cancers may have specific effects on sleep. When 32 patients with breast or lung cancer were compared with 32 age- and sex-matched normal sleepers and 32 otherwise healthy individuals with insomnia, different patterns of sleep disturbance emerged.[64] Lung cancer patients slept as poorly as those with insomnia, but they under-reported their sleep difficulties. Breast cancer patients slept

Table III. Percentages of poor and good sleepers reporting angina pectoris and cardiac arrhythmias in an epidemiological survey conducted in northern Sweden[67]

	Spasmodic chest pain and irregular heart beats	Spasmodic chest pain	Irregular heart beats	No problem
Men				
Slept well	3.0	9.9	7.9	79.2
Slept poorly	7.0	8.7	12.3	72.0
Women				
Slept well	2.3	7.0	8.2	82.5
Slept poorly	5.9	10.2	15.0	68.9

similarly to normal-sleeping volunteers. No significant differences in mood were found between lung and breast cancer patients, which makes the underestimation of the objectively verified sleeping difficulty in lung cancer patients more curious.

2.3.2 Cardiovascular Disease

A meta-analysis was performed to determine the effects of hypertension on quality of life as reported in published clinical trials of antihypertensive drug therapy.[65] All the studies included were randomised, blinded and compared active treatment with baseline (placebo or no treatment), with the patients as their own controls. Change was measured by self-evaluation and/or interviewer-assisted evaluation, standardised psychomotor/cognitive tests, or sleep laboratory observations. Nine published trials (1970 to 1990) involving 27 population groups (n = 1620) using 14 drugs from 6 pharmacological groups were analysed for 5 quality-of-life constructs: sleep, sexual function, psychomotor function, general well-being and mood. Significant improvement with treatment was seen for sleep, psychomotor function, general well-being and mood, while no effect could be determined for sexual function.

Symptom distress was measured in a US study of 175 patients (mean age 52 years; 85% men) awaiting heart transplantation.[66] The most frequent and distressing symptoms for such patients were tiredness, difficulty sleeping, difficulty breathing when active, and general body weakness. Patients with high levels of symptom distress were unable to work. Higher symptom distress correlated significantly with higher levels of stress

and functional disability, lower levels of life satisfaction, and diminshed quality of life.

In an epidemiological survey conducted in northern Sweden,[67] poor sleep was found to be associated with an increased occurrence of both angina pectoris and cardiac arrhythmias (table III) among men and women with reported sleep complaints. This increase in cardiac disease was found in those who had trouble falling asleep, those who frequently awoke during the night and had difficulty regaining sleep, and also in those with too early final awakening in the morning. Daytime sleepiness was also associated with increased cardiac symptoms.

2.3.3 Irritable Bowel Syndrome

A prospective, 1-month diary study was conducted in 23 adult patients with irritable bowel syndrome to examine quality of sleep.[68] At baseline, 74% of patients characterised themselves as 'poor sleepers'. Using pooled time series analysis, the study found a significant correlation between the quality of the prior night's sleep and 1) morning irritable bowel syndrome symptoms; and 2) end-of-day symptoms (the correlation was less strong but still significant). Morning symptoms appeared to rise or fall in close association with the quality of the previous night's sleep. The study reinforces the idea that irritable bowel syndrome symptoms are related to sleep disturbance.

2.3.4 AIDS

68 patients (mean age 38 years) with AIDS completed the Pittsburgh Sleep Quality Index, Beck Depression Inventory and Spielberger Anxiety State/Trait Inventory.[69] 61.8% of the patients were male and 38.2% were female. 79% of the pa-

tients had sleep disturbances as measured by the Pittsburgh Sleep Quality Index. This group had significantly higher Spielberger scores and Beck scores than those without sleep disturbances. There was also a significant relationship between caffeine consumption and sleep disturbances, but there was no correlation with the use of any other substance. No other variables, including stage of illness, were related to sleep problems.

In another trial, which examined noncurative treatments of HIV, the leading physical and mental symptoms contributing to health-related quality of life were fatigue, tiredness, weakness, malaise, depression, insomnia and anxiety.[70] It was again suggested that serious consideration should be given to these factors when plans for palliative treatments are being developed.

3. Discussion and Conclusions

Short sleep is not necessarily deleterious. In contrast, abnormally shortened or fragmented sleep can reduce an individual's performance and quality of life and be associated with the development of long term mood disorders. It is important to determine the cause of shortened sleep, as this can aid the choice of treatment strategies. The insomnias as defined in the ICSD are sleep disorders and, by their very nature, they reduce quality of life. The best current treatments are multimodal and involve both psychological and pharmacological techniques. Although disturbed sleep alone does not necessarily lead to a long term reduction in quality of life, it can cost national economies substantial sums through absenteeism and accidents. Sleep disruption or deprivation in normal volunteers leads to mood changes, the degree of which appears to be dependent on the personality of the individual; some data indicate that those with an external locus of control are more greatly affected than those with an internal locus.[72-77] Thus, disturbed sleep should not simply be discounted, as it may lead to long term psychiatric problems in those who are vulnerable. Longer term insomnia, i.e. sleep that is shorter or more fragmented than desired, is often associated with depression. This

fact alone provides a *prima facie* argument that insomnia causes a reduction in quality of life and that palliative measures should be applied.

The effects of nasal continuous positive airway pressure on quality of life have been measured in patients with the sleep disorder obstructive sleep apnoea.[78] This study showed that improvements of approximately 5.5 quality-adjusted life-years (the number of years of expected good health a patient can receive from active treatment) could be expected. Similar calculations have not been made for the insomnias, but the inclusion of sleep disorders in most quality-of-life measures suggests that treatment of insomnia would improve quality of life.

Sleep deteriorates with advancing age, primarily in parallel with the development of disorders associated with age. Sleep disorders *per se* also account for some sleep disruption. Hypnotic drug usage may act as an indirect index of this deterioration, but the use of hypnotics should not be abandoned if a reduction in quality of life would result.

Self-inflicted sleep disorders (e.g. those attributable to smoking, and the use of caffeine, over-the-counter sleep modifiers and alcohol) are common, as is work-related sleep disruption. With all of the above, quality of life could be improved with improved sleep education. If deterioration in health is associated with deterioration in sleep, quality of life is reduced. Direct treatment of the disorder causing sleep disturbance is the ideal, but, for many disorders, treatments are not particularly effective. The probable development of psychophysiological insomnia (and the possible subsequent development of mood disorders) that may follow uncontrolled and unresolved sleep disorders, together with the general reduction in quality of life, argues for an aggressive approach to the treatment of insomnia.

Overall, the section dealing with various medical disorders that reduce quality of life found varying responses, not all of which were intuitive. Active treatment of sleeplessness should consist of hypnotics that have a very good general safety

profile, such as zopiclone. Such agents should have been either tested or used widely in different clinical populations. Zopiclone has been investigated by postmarketing surveillance techniques in 20 513 general practice cases and confirmed to be a generally useful hypnotic.[79] In addition, it has also been used in special patient groups, e.g. those with renal or hepatic impairment,[80] or with respiratory impairment[81] and has also been found to be safe and effective in such groups.

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