Winter Fatigue and Winter Depression

Prevalence and Treatment with Bright Light

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Abstract

The aim of this thesis is to study prevalence of winter depressive mood and treatment effects of bright light for persons with winter fatigue and winter depression.

Study I is a cross-sectional survey of a random sample (N=1657) from the general population between 18-65 years of age in Dalarna, Sweden (latitude 60°N). Study II is a similar survey of 17-18 year old students (N=756) in the municipality of Falun. Approximately 20% of both samples report seasonal symptoms, mainly fatigue, lowered mood and increased sleep duration, appetite and weight.

Study III examines the effects of treatment in light rooms for persons from the sample in Study I (40 women, 10 men) with clinically assessed Seasonal Affective Disorder (SAD) or subclinical SAD (S-SAD). Subjects were randomised either to an experimental group receiving ten days of bright light treatment or to a three-week waiting-list control condition followed by bright light treatment. There was a >50% reduction of depressed mood in 13 of the 24 subjects in the experimental group, while none of the 24 controls reported a similar reduction. At the one-month follow-up, results were maintained and 39 of 47 subjects were improved >50%. Fatigue and excessive daytime sleepiness, which were high at baseline, were normal/below population norms for 39 of 47 subjects at the one-month follow-up. Mean values for the mental health aspect of health-related quality of life, which were low at baseline, improved and were close to norms at the one-month follow-up.

Study IV is a person-oriented subgroup/cluster analysis of the subjects in Study III. A common trait in all three clusters was a high level of fatigue hence the denomination ‘Winter Fatigue’ is used for the merged group. Even though the degree of depressive mood and daytime sleepiness differed between the subgroups, all three groups improved following bright light treatment.

The results suggest that an increase in fatigue and depressed mood during the winter season is common in the general population. Bright light treatment reduces depressive mood, fatigue and excessive daytime sleepiness and improves health-related quality of life in persons with winter fatigue and winter depression.

Keywords: prevalence, SAD, S-SAD, clinical trial, bright light therapy, light room, experimental design, fatigue, excessive daytime sleepiness, health-related quality of life, cluster analysis

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To my family

We don’t see things as they are, we see them as we are.

Anais Nin
List of papers

The thesis is based upon the following papers, in the text referred to by their Roman numerals.


IV Rastad, C., Ulfberg, J., Lindberg, P. Improvement in fatigue, sleepiness and health-related quality of life with bright light treatment in seasonal affective disorder (SAD) and sub-clinical SAD. *Submitted*.

All studies were approved by the Research Ethics Committee of the Faculty of Medicine at Uppsala University; Study I Dnr 01-240, Study II Dnr 02-348, Study III and IV Dnr 02-272.

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<td>Bright light therapy</td>
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<td>CI</td>
<td>Confidence interval</td>
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<td>ESS</td>
<td>Epworth sleepiness scale</td>
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<td>GS-score</td>
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<td>Health-related quality of life</td>
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<td>K-SPAQ</td>
<td>Kiddie-SPAQ, a child and adolescent version of the SPAQ</td>
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<td>MCS</td>
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<td>PCS</td>
<td>Physical component summary scale, one of the two summary scales in the SF-36</td>
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<td>SAD</td>
<td>Seasonal affective disorder</td>
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<td>S-SAD</td>
<td>Subclinical or subsyndromal SAD</td>
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<td>“SAD”, “S-SAD”</td>
<td>Inverted commas used when referring to results where prevalence estimates are based on self-report questionnaires such as the SPAQ and the K-SPAQ, and not a clinically assessed diagnosis of depression</td>
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<td>SF-36</td>
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<td>SPAQ</td>
<td>Seasonal Pattern Assessment Questionnaire</td>
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<td>VAS</td>
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<td>WLC</td>
<td>Waiting-list control group</td>
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Definitions

In the present thesis several different concepts are used for the same phenomenon. The main reason for this is the drift of meaning and definitions that occur through the passage of time.

*Seasonality* refers to the degree of seasonal variation in symptoms like energy level, mood, sleep length, sociability and appetite. Seasonality in the general population is continuously distributed, which makes it different to the categorical concept of depression. The concept of *winter depressive mood* includes seasonal symptoms of a winter type, while *mild* or *severe winter depressive mood* is used to describe differential levels of these symptoms.

*Winter depression* is a diagnosed depression and is equivalent to *Seasonal affective disorder (SAD)*. Both concepts are used interchangeably in the text. *Subclinical SAD (S-SAD)* is equivalent to *mild winter depressive mood* and the two are used interchangeably in the text. A *seasonal depression* is synonymous to SAD and is used in contrast to *nonseasonal depression*.

*Winter depression* and *winter fatigue* are proposed in the thesis as alternative concepts for *Seasonal affective disorder (SAD)* and *Subclinical seasonal affective disorder (S-SAD)*.
The sun has a far-reaching and profound effect on life on earth. The earth’s orbit around the sun and the earth’s rotation around its own leaning axis accounts for the seasons and the constant change of days and nights. It is essential for most organisms on earth - including humans - to adapt to these seasonal and circadian rhythms. Many human body functions fluctuate in relation to them, for example temperature, hormonal secretion, appetite and the timing of sleep and wakefulness. The internal body clock is adjusted to the 24-hour rhythm of the planet, but the relative length of this internal day and night differs to some degree between individuals. The change between light and darkness is one of the most important keys for synchronising the internal clock to the earths´ rhythm.

Because of its great impact on biology, it is not surprising that the sun, the light and darkness have been central symbols in many cultures and religions. In the ancient Greek creation myth, the gods of night and day, death, sleep and dreams, were all born out of Chaos. Thanatos who was related to death was the son of Nyx, the god of night and a twin brother to Hypnos, the sleep god. Helios, the sun god was often portrayed driving his sun-wagon over the sky. One of the most important in Greek mythology is Apollo, the god of light named “the shining”. He was also a god of music, poetry, truth (the oracles), science, healing and medicine and he was associated with the calendar. The famous words “know thyself” are said to be inscribed on the entrance to the temple of Apollo at Delphi.

Light has been associated with the divine, good forces and with positive emotions in European history for centuries, while darkness has been related to the evil forces, death and melancholia (1). Many of these ancient semantic connections are still present, as was shown in a Swedish study in which health professionals were interviewed regarding symbols related to life and death. Death was associated with old age, autumn, darkness, evening or night and a feeling of melancholy (1). Life on the other hand, was associated with youth, spring or summer, morning and midday, sunshine and feelings of joy, activity and sociability.

In modern western medicine, it is often assumed that diagnoses are objective and based on a common, known cause. However, in psychiatry most diagnoses are based rather on a categorizing of symptoms (2). Diagnoses in psychiatry are both necessary and useful, but at the same time they may be controversial and related to prevailing cultural ideas. In medical anthropol-
ogy, one focus is the cultural limitations of diagnostic categories. In such a study, the author investigated the cultural and social factors involved in Seasonal affective disorder (SAD). The conclusion was, that SAD is the result of a dichotomy between social time and the time of the body and nature; the body time is out of synchrony with social time (1). In other societies, the seasons may be better integrated into the common system of rituals and beliefs, which makes the gap between the natural and social time smaller.

One should keep in mind that seasons are very different in different parts of the world. In the northern hemisphere, the seasons are characterized by large differences in duration of daylight and in temperature. Closer to the equator the daylight lasts about twelve hours all year round and the temperature is more even throughout the year. Even though the seasons on different parts of earth differ in character, the specific seasons may be more or less related to certain emotions and behaviours. There are some indications that in western countries negative affect is primarily related to the winter (cold and dark) season, while in several non-western countries negative affect is related to the summer (hot and sunny) season (3). In a Bolivian society for example, the dry season was a time for feasts, marriage, intense social life and rest from work, while the wet season was a time for sadness, for remembering the dead – and for work (1). Sadness was a natural phenomenon during the wet season and to a certain extent was shared by all in the society.

The psychological and cultural perspectives on seasons and mood may still be of importance in modern life. Even though few worship a sun god, many of us experience pleasure and positive feelings spending time outside in the daylight or in the sunshine, sunbathing when possible or longing for the summer vacations during the dark periods. Rituals do change as time passes, but the festivals during the peak of darkness (Christmas) and the peak of light (midsummer) remain. In November and December, there are special lights in the windows in almost every home throughout Sweden, a common and shared ritual that probably makes it easier for us to endure the darkest period of the winter season.

The fundamental assumption, that physics, biology, psychology and culture are inseparable and interact, is a personal starting point for this thesis. Does that mean that SAD is merely a cultural phenomenon, invented by researchers and clinicians during the late 1980’s, as suggested by some persons whom I met in clinical practice? No, I do not think so. Emotions are rooted in both biology and culture, and diagnoses exist within a specific cultural and medical context. Remembering that, we are free to further explore – in this case – prevalence of seasonal depressive symptoms and the treatment of those symptoms with bright light.
Introduction

Seasonal symptoms in the population during the winter are common but prevalence studies performed in Sweden were lacking when this project was planned. Bright light therapy (BLT) in the form of treatment in light rooms for patients with seasonal depression was used in clinical research in Sweden in the 1980s (4-7) and further introduced in health care in several Swedish hospitals in the 1990s. More recently, the scientific evidence for this treatment was not considered sufficient by the Swedish Council on Technology Assessment in Health Care, which called for more controlled, clinical studies (8, 9). The present thesis was initiated in order to investigate prevalence of winter depressive mood and the treatment effects of bright light in a group of persons with Seasonal affective disorder (SAD) and Subclinical SAD (S-SAD). An overview of the clinical picture, prevalence, possible etiological factors, treatment with bright light and clinical studies is presented below.

The clinical picture

Seasonal Affective Disorder (SAD)

In the classic study by Rosenthal and co-workers (10), the authors proposed a definition of winter SAD which is still basically the same, i.e. a history of major depression for at least two consecutive years during autumn or winter with remission during the following spring or summer, absence of other psychiatric disorders and no seasonally changing psychosocial variables that could account for the seasonal symptoms (such as work stress) (11). In addition to typical depressive symptoms (such as diminished interest and pleasure, fatigue and feelings of worthlessness), there are some common atypical symptoms, such as increased sleep length and appetite, carbohydrate cravings and seasonal weight gain (11).

The diagnostic criteria for SAD were published in the psychiatric diagnostic manual DSM III in 1987 and in the later 1994 version as a specifier of either recurrent or bipolar major depressive disorder with a seasonal pattern of depressive episodes (2). SAD was not considered a separate diagnostic entity in the DSM-IV, since it was not clear whether it represents a distinct affective disorder, a subtype of recurrent affective disorder or a more severe form of a widely distributed population trait (12). However, in the DSM-IV
version, two changes were made to the original Rosenthal criteria; other (comorbid) psychiatric diagnoses were accepted and seasonal depressive episodes were to substantially outnumber nonseasonal episodes.

Even though there are few reports on the presence of comorbid disorders, the results indicate that it is common in SAD (12). In a recent study (abstract only) 66.3% of the SAD patients had a comorbid disorder, most common being different types of anxiety disorder (13). The seasonal pattern of the symptoms is central to the diagnosis; there should be deterioration during the autumn and/or winter season followed by an improvement (preferably a full remission) during the summer.

In one of the long-term follow-up studies of SAD patients, results showed that 2-5 years following light therapy 26% had a stable SAD diagnosis, 44% changed for the better (subclinical SAD), 20% had not relapsed and 10% changed into other depressive or anxiety disorders (14). In another study in which SAD patients were interviewed, results showed that 5-8 years after the initial diagnosis 38% had a stable diagnosis, between 6% and 11% had subclinical symptoms, 18% had not relapsed and 30% had a nonseasonal depression (15).

Subclinical SAD (S-SAD)
Kasper and co-workers (16, 17) defined subclinical SAD (S-SAD), a mild form of SAD with similar but less impairing symptoms. These authors identified a group of subjects with winter difficulties who neither met criteria for a major depressive disorder nor sought treatment for these symptoms, but nevertheless experienced symptoms similar to those found in SAD. There are preliminary signs for the existence of this mild form of SAD but the definition of S-SAD is problematic and needs clarification (18, 19). Since S-SAD is not a diagnosis, it is not included in the DSM-IV. There are several reports of a proportion of healthy personnel without any previous seasonality, experiencing seasonal symptoms equivalent to that of S-SAD while working in the Antarctic over the winter season (20).

Symptoms described by the patients
Both clinical experience and the literature suggest that one of the main complaints from persons with SAD and S-SAD is that of an overwhelming feeling of fatigue, a profound lack of energy or tiredness. This symptom often exceeds that of lowered mood (21). Even though depressed mood is one of core symptoms it is not always present, especially not in S-SAD. Many persons with SAD and S-SAD experience difficulties in performing daily activities due to depressed mood and fatigue and even the simplest task may seem almost impossible to carry out (11). Many report becoming less sociable and preferring solitude to the company of others. There is a general low interest in activities that are usually interesting or pleasurable. Feelings of worry, anxiety and irritation are common and sexual interest may be markedly re-
duced. From clinical experience there are reports that the capacity for work is affected leading to some patients being seasonally sick-listed.

The pronounced increase in sleep length can be problematic, especially for those persons who want to sleep for ten, twelve or more hours per 24 h day/night cycle. In spite of sleeping longer than usual (or feeling the need to do so) the person feels tired or drowsy during the day. Others report suffering more from insomnia, with difficulties initiating sleep, maintaining sleep or early awakenings (11). There may be a pronounced delay of daily rhythms; the person feels slightly more alert during the evening and therefore goes to bed later than usual, with the accompanying difficulties in getting up the following morning. The feeling of drowsiness often lingers on until lunchtime the following day. Some persons describe an increased craving for sweets and all types of carbohydrate-rich food, which can result in a substantial seasonal weight gain.

The length of the depressed period differs from individual to individual; for some it is a month or two, for others it is a longer period that starts in early autumn and ends in late spring (11). Some patients report that they start worry about the coming fall-winter period early in the summer when they know that the days are starting to get shorter again. Still others report a heightened sense of wellbeing and energy during the summer, with an increase in activity and sociability and a marked reduction in sleep length. The pronounced difference in mood and activity between the seasons constitutes a problem in itself, putting a strain on personal and work relations. It may be difficult for family members, friends and workmates to understand why a person is suddenly so changed.

Prevalence

The study of SAD prevalence in the population has been heavily dependent on the Seasonal Pattern Assessment Questionnaire (SPAQ) (22), a retrospective self-report questionnaire which has been used in a large number of epidemiological studies since the 1980’s (23-25). Kasper and co-workers introduced the cut-offs on the SPAQ used for defining SAD and S-SAD (17). The procedure of how to calculate prevalence figures on the SPAQ is described in the Methods section, where the measures are presented. It is now commonly agreed upon that the SPAQ reflects seasonal mood changes or “seasonality” and not diagnosed SAD (24). Therefore, inverted commas are used in the text for “SAD” and “S-SAD”, to indicate that reported prevalence rates are based on self-reports and not diagnosed depression. Levitt and co-workers found that the SPAQ over-estimated prevalence of clinically confirmed SAD between 2 and 4 times (26, 27).

A review of results from prevalence studies was presented by Magnusson in 2000 (25). The prevalence of “winter SAD” reported in studies using the
SPAQ, vary between 1% and 9% (community based studies or studies performed in primary health care in Europe, the United States and Canada) (25, 28, 29). Corresponding figures for “winter S-SAD” vary between 3% and 19% (25, 28, 29). The use of different criteria for defining “SAD” and “S-SAD” is one of the factors behind the differences in reported prevalence rates. Female to male ratios vary between 1.5 to 1 and 3.5 to 1 (Europe, the United States and Canada) (25, 30, 31).

Clinically assessed (telephone or face-to-face interviews) estimates of SAD vary between 0.4% and 2.4% in general population samples (Canada, the USA and Great Britain) (26-28, 32, 33). Prevalence is slightly higher in samples from primary health care (3.5%) (28). The proportion of persons with a seasonal depression was estimated at approximately 10% of all persons with a major depressive disorder (26, 27).

In one study on prevalence of winter depressive mood among children and adolescents between 9 and 19 years of age, Swedo and co-workers reported that between 1.7 and 5.5% were identified as probable SAD cases (34). Reports of seasonal changes in mood and behavior were common and more frequent among girls compared to boys in a sample of students in the 7th grade (13-14 years of age) and 9th grade (15-17 years of age) in Finland (35). At least one seasonal symptom during the winter (such as the child eats or sleeps more, is tired, irritable or sad) was reported by 48.5% of the parents having children in the 4th, 5th and 6th grade (9-11 years of age) (36).

**Latitude and prevalence**

Whether or not prevalence of seasonal symptoms varies in relation to latitude has been a topic of repeated discussions over the years. However, two reviews have concluded that the association between latitude and prevalence is unclear and if existent, is rather weak (37, 38). Results from an unpublished Swedish study including 380 persons found no differences between the northern (Kiruna, lat. 67.8°N) and southern (Trelleborg, lat. 54.4°N) parts of Sweden (39). It may be that photoperiod (day-length) rather than latitude (distance to the equator) is the variable of interest. Day-length varies in a consistent way over the year in all countries, but climatic factors (such as hours of sunshine and temperature), latitude and photoperiod are highly interrelated. So far, we have not been able to clearly differentiate between these variables (40, 41). The onset of winter SAD was shown to be associated to photoperiod and at very high latitudes, prevalence is lower than assumed (41). Therefore the relation between latitude and prevalence may not be linear.
Possible etiological factors

The biomedical perspective

The etiology of mental depression is not fully known, and even less is known about the different subgroups such as seasonal depression. There is a variety of more or less interrelated hypotheses regarding the etiology of seasonality and Seasonal affective disorder (SAD). Overviews of these have been presented elsewhere (42, 43).

When it was reported in the 1970s that bright light exposure of the eyes during the night could suppress melatonin secretion in healthy subjects, the understanding of biological rhythms in humans took a major step forward (44). Light and darkness were established as one of the major synchronizers of biological rhythms and this discovery led directly to the use of bright light as a treatment for SAD (45, 46). As discussed in the overview by Lam and Levitan (42), it was later found that the nocturnal duration of melatonin secretion in humans, reflected changes in photoperiod. This was especially pronounced in patients with SAD and therefore, it was suggested these persons are more likely to respond to seasonal photoperiodic signals than others (42). Depression was associated with day-length and amount of sunshine in persons with SAD (47).

Melatonin is sometimes called the “chemical signal of darkness” and it is very sensitive even to short flashes of bright light. It is released from the pineal gland into the blood system and sends its message of time-of-day and time-of-year (season) to the body (48, 49). Even though melatonin has not been unambiguously linked to an anti-depressive effect in SAD (50, 51), an optimal time-point for treatment with bright light in the morning was established in relation to the melatonin cycle (52).

Some researchers have looked upon SAD from an evolutionary perspective. The onset of the vegetative symptoms (low energy, long sleep, weight gain) might naturally be related to photoperiod and the need for conservation of energy during certain seasons in order to favor reproduction and survival (53, 54). While once an adaptive function, in contemporary modern life it rather presents as an unwanted temporary state of depression (54).

Disturbances in the circadian (day and night) rhythms were early proposed as a major factor behind SAD. If SAD is the result of a phase-delay in relation to the external clock or other rhythms, then bright light in the morning could be used to phase-advance the delayed rhythms (55). There is some evidence to support a circadian phase delay in SAD, but results are not consistent (52, 56). It may be that some but not all patients with SAD have delayed circadian rhythms (43).

Melatonin and serotonin are two of several hormones involved in the process of adjusting the inner physiological processes and behavior to the corresponding outer day and night and the seasons. There is a biochemical link between them and their levels vary in opposite ways according to the length
of the day and the seasons (57). Brain serotonin is involved in the regulation of physiological functions that vary with the seasons, such as eating, sleeping and energy balance. In a study of healthy subjects, the production of serotonin in the brain was directly related to the amount of bright sunlight (58). Serotonin transporter binding potential was shown to vary with the seasons and with hours of daily sunshine (59). The lowest levels of serotonin were found during the fall and winter season and the highest in spring and summer. Patients with SAD in remission after treatment with bright light experienced a clear relapse of depressive symptoms following tryptophan depletion (tryptophan is precursor to serotonin) (60). These results and others clearly suggest a serotonergic mechanism in SAD. Other, although indirect data in favor of the serotonergic hypothesis, is the positive effect of antidepressive medication in SAD (61). Other monoamine neurotransmitters like dopamine may be involved but less is known about the role of these in SAD.

Conscious vision is not the only function of the human eye. Recently, a new photopigment, the melanopsin signaling pathway, was discovered in the retina (62). It is involved in a non-visual photic response system that affects our response to light, circadian rhythms, behavior, alertness, sleep and cognition. This newly discovered pathway was shown to have a peak sensitivity (for plasma melatonin suppression) in the blue region of the visible spectrum of light, which also was shown to be the most effective part for enhancing alertness (63). Another recent study, showed that 5% of a sample of SAD patients had a melanopsin gene variant that possibly constitutes a genetic risk factor for SAD (64). If retinal receptor sensitivity is lower in some patients with SAD, then this may be one of the factors explaining the need for extra light during the winter season.

Higher than expected rates of affective illness among relatives of persons with SAD and corresponding studies of twins indicates that there is fairly strong evidence for a genetic factor in both SAD and seasonality, as discussed in an overview of biological aspects in SAD (43). It is now widely recognized that there is heterogeneity in the etiology of SAD and seasonality. An integrative approach involving biological rhythms, neurotransmitters, genetics and the potential role of the eyes is more likely to explain SAD than any single factor (43). A dual-vulnerability hypothesis has been proposed, where SAD is the result of a combination of a vulnerability to both seasonality and depression (18). Different combinations of these factors would then explain both seasonality (high loading on the seasonal factor only) and SAD (high loadings on both factors).

The biopsychosocial perspective
A biopsychosocial model for disease was first presented during the 1970’s, as a complement to the biomedical model (65, 66). The basic idea that biological, psychological and social factors are interrelated and affect each
other, is now widely recognized. However, in SAD less is known about the impact of psychological and social factors than biological factors.

**Personality, social and cognitive factors**

One group of studies have focused on the role of personality factors in winter depression. Results showed that SAD patients had higher scores compared to norms in the neuroticism dimension (a broad concept of a range of negative affects in the five-factor model of personality), but lower than those found in patients with nonseasonal depression (67). Patients with SAD were also characterized by high scores on the openness dimension, which indicates a higher receptivity and appreciation of unconventional ideas, new experiences, aesthetics, a high level of curiosity and a tendency to experience more intense emotions (67, 68). This was a relatively stable trait since it was found during both the winter and summer seasons (when depressed and when feeling well).

In a Swedish study, Pendse and co-workers found that SAD patients’ clinical background and social situation was similar to a group of patients with nonseasonal depression, who had attempted suicide (69). Both groups had weak social networks compared to healthy controls and social impairment was considerable among SAD patients. In another study by Michalak and co-workers, SAD was associated with lower occupational and cognitive impairment and less psychiatric intervention than nonseasonal depression (70). Contrary to this, it was demonstrated by Pendse and co-workers, that SAD patients had a more severe psychopathology than in patients with nonseasonal major depression who had attempted suicide (71). These contradictory results may be in part explained by study setting; the latter study by Pendse and co-workers was performed in a psychiatric clinic, while the former study by Michalak and co-workers was performed in primary health care.

There are some studies that provide preliminary evidence for the role of cognitive factors in SAD, for example negative thought patterns and rumination (focusing on symptoms) (72). Spatial memory and learning was impaired in SAD compared to healthy controls and improvement in the tests were seen after recovery (73). In a naturalistic study, persons with SAD were followed prospectively as depressive symptoms emerged during the winter. Low self-esteem and poor perceived social support, was related to an earlier onset of the depressive symptoms (74). Experiencing more negative life events and low levels of social support were predictive of high seasonality (75).

**Health-related quality of life**

Health-related quality of life (HRQoL) concerns the impact of illness on an individuals’ life. There is no consensus on the definition and subsequently, measures of HRQoL range from one-dimensional and disease-specific to multi-dimensional and generic. Despite the lack of agreement on the definition, measures of HRQoL are used for examining and comparing the impact
of different psychiatric and somatic conditions, following different treatments and between countries (76).

There are some studies on HRQoL in patients with Seasonal affective disorder (SAD). Michalak and co-workers (77) found that patients with SAD were markedly impaired in their perceived HRQoL during the winter months and significantly improved during the summer months. In another study of patients with SAD, treatment with bright light was associated with improvement in the perceived HRQoL (78). The authors recommended that broader indices of patient outcomes such as measures of health-related quality of life were to be included as outcome measures in clinical trials of SAD (78).

**Fatigue and excessive daytime sleepiness**

Fatigue and sleep problems are frequent but rarely addressed symptoms in clinical research in SAD and S-SAD. Fatigue was described for example in an early article published in 1952, in which most of the features were outlined (79). It was described as a psychological symptom and a sort of “negative appetite” for activity. Fatigue is a multidimensional and non-specific symptom that is common in a variety of both psychiatric and somatic disorders (80). For example, between 73% and 97% of outpatients with depression report fatigue (81). “Daytime tiredness” was reported by 84% of patients with winter SAD (82). A common definition of (persistent) fatigue is that of an overwhelming sense of tiredness and lack of energy, that is not relieved by rest or sleep (83). In fatigue questionnaires, it is common to divide fatigue into mental and physical fatigue (84). In a study of neuromuscular disorders, physiological fatigue was defined as an exercise-induced reduction of voluntary muscle force and experienced fatigue as a difficulty in initiating or sustaining voluntary activities (85).

In one of the more general theories of fatigue, the Fatigue Adaptation Model, Olson et al (86) suggest that fatigue may be viewed as a behavioural marker for an inability to adapt to stress (87). In this theory, fatigue is considered one of several specific states along a continuum labelled adaptation. Each state along this continuum can be characterized in terms of sleep quality, cognition, stamina, emotional reactivity, control over body processes and social interaction (86). One consequence of the theory is that psychological or other interventions such as the reduction of stressors may be used to alleviate fatigue. Whether or not this theory is relevant to the treatment of SAD remains to be proven, but it is an interesting option for future studies.

The neurological basis for fatigue has not been established, but there are several possible explanations involving neurotransmitters in the brain (88). Some support for the involvement of the stress system in SAD was reported by Stahl et al (88). In that study, patients with SAD (and atypical depression) were found to have a hypoactive or downregulated stress system. A hypoactivity of the core stress system, which promotes arousal and diminishes
food intake could explain the fatigue, hyperphagia and hypersomnia, which are common in SAD. In a study of stress and coping strategies, persons with seasonal and nonseasonal depressions used fewer acceptance and more avoidance coping strategies compared to healthy controls (89). Persons with seasonal depression however, used more light-related and season-specific strategies than persons with nonseasonal depression and healthy controls.

Excessive daytime sleepiness is defined as an increased drive to fall asleep (at inappropriate times) and is a condition that can be relieved by sleep (83). Results from a study in patients with SAD showed that treatment with bright light reduced both depression and daytime sleepiness (90). There are some indications that patients with SAD in winter show decreased sleep efficiency and slow-wave delta sleep, which was reversed in summer and by treatment with bright light (91).

Studies among patients with sleep disorders suggest that fatigue and sleepiness are partially overlapping but not identical phenomenon and therefore, need separate assessments (83). There is some evidence that women tend to report a higher general feeling of sleepiness and fatigue, while men report higher scores on measures of sleep propensity (92), which is why it seems reasonable to include both a fatigue measure and a measure of daytime sleepiness in a clinical trial of treatment with bright light.

Light and how it is measured

In bright light therapy, one may consider the definition of “light” and “bright light”? What is needed to make bright light a treatment or a “therapy”? These issues are related to several factors; to the physical aspects of the light source, to the light that actually reaches the retinal receptors and the further transduction of neural signals to the brain, to the physical environment and the experience of ambient light and colours.

Light is a type of energy, an electromagnetic radiation that can easily travel through space. Visible light consists of wavelengths ranging from 380 to 760 nanometres, which is only a small part of a much broader electromagnetic spectrum. The eye differentiates between these wavelengths through the sensation of colours (93). The photons, the particles responsible for electromagnetic phenomena, are absorbed by retinal photopigments and neural signals are then transmitted to various parts of the brain (45). The sensitivity of the eye for different wavelengths varies and is different during the day and night. What the eye can perceive of the light from any type of light source varies with the distance, the direction, the position and other factors like gazing.

Photometry is the science concerned with the measurement of light in terms of how it is perceived by the eye. There are a number of different units used in photometry, for example lux and candela (94, 95). Lux indicates the
amount of light that is falling on a surface, while candela/m² is the perceived brightness of a surface. Both units are used for reporting light intensities used in clinical trials of treatment with bright light. There are several sources of possible measurement errors when measuring light intensities, for example the technical equipment, the direction of the measurements (device pointing towards the floor, the roof, towards the light or away from it, “as the eye sees” or any other direction) and the position in the room (level of standing, sitting, different parts of the room) (93). Therefore, a trained technician may be needed, with the knowledge of how to carry out the measurements in a reliable way in several, fixed locations and directions.

Architects have long recognized that type of ambient light affects mood and the experience of colours in a room. The interplay between light and shadow is essential for how we apprehend space, form and structure. Ambient light can also be described according to its “temperature”, whether it is cold, neutral or warm. Kelvin (K) is the unit of colour temperature. Different types of light sources vary considerably in temperature and different brands of the fluorescent tubes that are used in treatment with bright light vary correspondingly.

There is no artificial light that exactly resembles daylight and different types of artificial light also differ from each other. The RA-index describes the ability of a light source to reproduce colours in relation to natural daylight and varies between 0 and 100 (daylight). We do not know if and how these quality aspects of light can directly affect the results of treatment with bright light, but they certainly affect the experience of the light and the room.

The type of light recommended for treatment with bright light has been and still is, white light; i.e. full-spectrum fluorescent or cool-white fluorescent light (31). An RA-index close to 90 or over, about 5500 K and an even spectral power distribution, is recommended by several commercial companies. There are a number of studies investigating what specific wavelengths are most effective in relieving depressive symptoms and findings indicate that the red parts seem less effective compared to the blue parts, but the recommendations to use white light is, for the moment, not changed (31, 96, 97).

**Bright light therapy**

**Light intensity, duration and timing of treatment**

In one of the first studies of bright light therapy (BLT) published in 1984, the light intensity used was 2500 lux with a treatment duration of 3 hours both before dawn and after dusk (10). However, twice-a-day treatments were time-consuming and rather impractical and later, when it was found that this did not seem crucial to the effect of BLT, the recommendations changed. In the first review of BLT for SAD published in 1989 the prescribed duration was changed to treatments for 2 hours daily (98). Since improvement is often
seen during the first week of treatment, the initial studies recommended one-week treatment periods. Later it was found that the response rate increased with treatment periods of two weeks (99). A few studies have investigated longer treatment periods than two weeks, with treatments lasting three to five weeks (100).

In several clinical studies, the effects of “bright light” have been compared to a control condition of “dim light”. Unfortunately, there are no norms for what is considered bright or dim light and subsequently, these differ between studies. One suggested definition of “bright light” is light >2000 lux and of “dim light” <500 lux (31). However, positive antidepressive effects were found with lower light intensities (1500 lux or less) (6, 101) and it is now known that light affects the body at lower illuminance levels than 200 lux (45). Therefore, the dim light conditions used in some previous studies may not be the optimal placebo condition that it was intended to be. In spite of the inconsistencies in the definitions of bright and dim light, the general finding is that bright light is more effective than dim light (31). There seems to be a light intensity x duration relationship, which indicates that the effect of 2500 lux for 2 h is equivalent to 10000 lux for 30 min (98).

The optimal time of the day for the treatment has been investigated in several studies. In spite of some inconsistencies in findings, the effects of morning light was found to be superior over evening light (102). There are no studies showing that evening light is superior to morning light, but some have shown no difference between the two (6, 103, 104). Since light treatment affects the daily rhythms (can cause phase-delays or phase-advances), the effects of bright light for a specific individual may partly depend on her/his pattern of daily rhythms, if she/he is a morning lark or an evening owl (102). The difference between individuals may be large, since the circadian rhythms differ by up to 6 h between individuals (105). This is in agreement with a previous Swedish study of 63 patients being treated in a light room, in which melatonin was measured from 20.00 p.m. until 08.00 a.m. the following day (50).

To summarize, the present recommendation for treatments with 2500 lux is two hours daily for two to four weeks in the morning (31).

Two different settings; light boxes and light rooms

Many clinical studies evaluating the effects of bright light therapy (BLT) have used light boxes. However, there are differences between the use of a light box and the light room setting as illustrated in Figures 1 - 2. The light box is a portable device and can be used for example at home. The light room is situated at an outpatient or inpatient clinic with staff and other patients present. For many patients, treatment in a light room is more time-consuming compared to treatment with a light box at home, mainly because of the traveling distance to the clinic. In practice, especially for treatments in light rooms, all patients must consider the total time needed for treatment in
relation to everyday family and work schedules. On the other hand, in clinical experience we find that many patients appreciate having the time for personal use while sitting in the light room. At home there may be other members of the family to take into consideration. It is obvious that several variables in addition to the light itself may contribute to treatment effects in both settings, but in different ways.

**Light boxes**

In this thesis, the light box is defined as a portable light therapy device used in the evaluation of light treatment or in the treatment of mood disorders. There are different types of light boxes offered for sale to private persons, which can be used at home, at work or at a clinic. The light intensities (as given by the manufacturing companies) vary between 2500 and 10000 lux. The instruction when using a light box, is to sit slightly oblique in front of the box at a certain distance (for example 50 cm) with eyes open but without looking straight towards the light.

When using a light box, the light intensity is strongly influenced by the distance between the eyes and the light source (106, 107). In an early study, proximity to the light source and gazing was systematically varied in order to study the discrepancy between perceived and transmitted light (106). Subjects exposed to light boxes emitting 10000 lux at best perceived only 20% of the transmitted light. This figure dropped rapidly to between 1% and 2% as the subject moved away slightly from the original position. The authors concluded that the figures for light intensities given by commercial companies should not be taken as a guide to the effective levels of perceived illumination and that it was reasonable to assume that the perceived illumination is between 5% and 15% of the reported illumination, when a light box is used (106).

When the treatment is carried out in patients’ homes, it is obviously difficult to know if subjects comply with the prescribed treatment regimen. Most studies have relied solely on subjective reports on compliance and little research has been focused on the extent to which subjects in studies of BLT are “doing what they are told to do”. A recent study indicated that the mean duration of the light box actually being turned on was 59.3% of the prescribed time, but the figure was higher for those completing the study (83.3%) compared to the drop-outs (107). Self-reports of exposure time were not related to objectively estimated duration of light box use.

It is clear that the above findings should be taken into account in the planning of future studies if light boxes are to be used.

**Light rooms**

The light room was originally designed in the 1970s at the Karolinska Institute in Stockholm for clinical research purposes in order to obtain accurate measurements of the light dose in different experiments concerned with the
Figure 1. Illustration of a common treatment setting for a light box when used at home or in an office (photo C. Rastad).

Figure 2. Illustration of a treatment setting for a light room. The picture is taken in one of the four light rooms used in the project, the former light room in the Movement- Art- and Music Therapy unit at the Psychiatric outpatient clinic in Falun. (photo U. Palm).
hormonal effects of light in humans (108). This concept was further evolved into light rooms for treatment studies in the early 1980s in order to improve the control of compliance and to be able to treat a group of patients at the same time and under similar light conditions 1.

The light in the rooms was designed to be indirect, i.e. more evenly distributed in the room, which reduces the risk of a variation in light intensity during treatment. The walls and ceilings were painted white and the furniture was light-colored. Patients sat comfortably in armchairs wearing white robes that covered their ordinary, often darker clothing 1. A further reason for using light rooms instead of light boxes in clinical research was the possibility of following the symptoms of each patient on a daily basis. It was also clear at an early stage that latent bipolar depressive patients might swing into a manic phase after 3 to 4 days of light treatment. When the patients were followed with a clinical examination on a daily basis, a full manic phase could be prevented. This would not have been possible if treatment had been given in their homes 1. While in the light room, patients can engage in calm activities like reading or handwork. Some prefer to be silent, others engage in conversations with each other or with the staff. Health care personnel may be present in the light room during parts of the treatment.

The light rooms used in the present study are basically the same as the light rooms that were constructed during the 1980s and 1990s at the Karolinska Institute. It should be noted however, that there is no standard for the light intensities to be used in light rooms. A light intensity of 2500 lux is common, but there is a variation between approximately 1500 and 5000 lux (from the authors own clinical experience).

The majority of the light rooms in Swedish health care are situated in psychiatric clinics, but in some cases also in primary health care or at sleep disorders centers. A recent estimate showed that 39 out of 99 responding psychiatric departments provided BLT, which indicates that it is a fairly common treatment in Sweden (9). However, the large interest in BLT from the mass media during recent years, far exceeds the actual availability of the treatment, due to traveling distances to the clinic and the fact that treatment in a light room is usually carried out for between 1 and 2 hours early in the morning for ten consecutive days (weekdays).

**Side effects and risks**

There are no reports of any severe risks associated with bright light therapy (BLT) (8), but there are some generally mild and transient side effects. The most common are eye strain and headache, while less common are feeling “wired”, nausea, irritability, sweating, palpitations, muscle pain and rashes

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1 L. Wetterberg, personal communication 2009-01-11
(31, 109, 110). There are no absolute contraindications for BLT, but there are case reports regarding the risk of triggering a manic episode in patients with a bipolar disorder (111). There is some concern regarding the risks for retinal damage, mainly from the UV and blue parts of the spectrum (112) but long-term use of BLT has not been reported to cause ophtalmological damage (31, 113). In patients with retinal disease, a systemic disease which may affect the retina, or a patient that is currently taking medications that have a photosensitizing effect (e.g. hypericum, tetracyclines, lithium, antipsychotics) an eye examination or consultation is recommended prior to treatment (31, 112).

Clinical studies

In all there are about 70 controlled clinical studies of bright light therapy (BLT) (61) but the majority of these are considered to have serious methodological flaws (9, 114). In one of the reviews of controlled clinical trials of BLT, it was concluded that there is some evidence for the efficacy of BLT, with effect sizes equivalent to most antidepressant pharmacotherapy trials (114).

A recent double-blind controlled study of 96 patients with SAD showed that both treatments with BLT and antidepressants were effective in reducing depression (61). The patients were randomly assigned to either BLT and a placebo capsule or placebo light and fluoxetine. The study duration was eight weeks. Post hoc testing showed that BLT resulted in lower depression scores compared to medication after 1 week of treatment. Fluoxetine was superior to BLT in the subset of patients with more severe depression at baseline. In another study using actigraphy (a wrist-worn device measuring motor activity) patients with SAD were shown to have a 43% lower activity during the day and lower sleep efficiency than healthy controls (115). Four weeks of BLT led to improvements in sleep efficiency and increased daytime activity in the SAD patients.

A positive effect of BLT in subjects with S-SAD compared to healthy controls was found in an early study by Kasper (16). In a study with a retrospective design performed in a specialized SAD clinic in Canada, both persons with S-SAD and SAD improved following BLT (18). The S-SAD group had the best response to BLT. In another study with an open design, the response rates were similar in subjects with SAD and S-SAD following BLT (19).

There has been limited research on the effects of treatment in light rooms. In one such study, Thalén and co-workers showed, in a study with an open design, that patients with seasonal depression (N=68) improved more than patients with nonseasonal depression (N=22) (6).
Intentions and scope of the present thesis

Even though there are several prevalence reports of winter depressive mood ("SAD" and "S-SAD") from different countries (25), prevalence in the general Swedish population was largely unknown when the present thesis was planned. There was also limited knowledge of prevalence among children and adolescents. According to the Swedish Council on Technology Assessment in Health Care (8) the evidence for bright light therapy (BLT) was insufficient and this indicated a need for further controlled clinical studies.

There are indications that bright light is effective in reducing depressed mood both for persons with Seasonal affective disorder (SAD) and for persons with subclinical SAD (S-SAD). Since a common complaint among these persons is lack of energy and sleep problems, measures of fatigue and excessive daytime sleepiness should be introduced and used. In order to gain a better understanding of the impact on general health perceptions, measures of health-related quality of life should be used to study how mental and physical health perceptions change following treatment. Furthermore, it is of interest to explore subgroups among persons with winter depressive mood ranging from mild to severe, and to evaluate any differential treatment effects.

The majority of clinical studies have used light boxes and the treatment has generally been carried out in patients’ homes. Bright light treatments at home and in a health care environment certainly have the bright light in common, but differ in several other central aspects. Therefore, results from studies using light boxes cannot immediately be applied to settings in which light rooms are used. To improve the evaluation of treatment in light rooms, more basic designs for controlled trials in such settings should be considered, for example inclusion of untreated waiting-list controls. It is perhaps the most basic research question to ask, whether a “treatment package” is effective or not. The “treatment package strategy” is later to be followed by other designs with the specific aim to analyse what components of a particular treatment are effective and how to maximize the treatment effects (116).

A few comments should be made on issues not addressed in the thesis. Bright light treatment (BLT) has been used in a limited number of studies to treat other disorders, many of which may have disturbed circadian and seasonal rhythms in common (117), for example persons with dementia (118), bulimia (119), delayed sleep phase syndrome (120), adult attention-deficit hyperactivity disorder (121), nonseasonal depression (122) and children with SAD (123). There are also other types of light treatment, for example gradual dawn simulators and light visors, which are not included in the thesis. Furthermore, even though treatment options for SAD include both BLT (10, 98, 114) and anti-depressive medication (61, 124-126) and possibly also cognitive-behavioral therapy (for the latter results are promising but still preliminary) (127), only treatment with bright light is the focus of this thesis.
The overall aim of this thesis is to study prevalence of seasonal symptoms in
the general population and the effects of bright light therapy in persons suf-
fering from SAD and S-SAD.

Specific aims were:

• To estimate the prevalence of self-reported seasonality in
  adults and adolescents and describe some of the symptoms
  (Study I and II)
• To evaluate short- and long-term effects of bright light ther-
  apy on depressed mood in persons with SAD and S-SAD
  (Study III)
• To evaluate treatment effects of bright light therapy for
  clinical symptoms of fatigue and sleepiness and self-reported
  health-related quality of life in persons with SAD and S-
  SAD (Study IV)
• To explore and validate empirically derived subgroups in the
  sample receiving bright light therapy and to study any differ-
  ential treatment effects in the subgroups (Study IV)
Methods

The data collection started in December 2001 and was completed in April 2004. An overview of the studies, designs and samples in the thesis are presented in Figure 3. The sample in Study III and IV were recruited from the sample in Study I.

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<tbody>
<tr>
<td><strong>Design:</strong></td>
<td>Cross-sectional survey design</td>
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<tr>
<td><strong>Subjects:</strong></td>
<td>A proportionally stratified (age, gender, home municipality) random sample of the general population between 18 and 65 years of age from five municipalities in Dalarna, N=1657</td>
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<tr>
<td><strong>Data:</strong></td>
<td>Retrospective</td>
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<tr>
<td><strong>Design:</strong></td>
<td>Cross-sectional survey design</td>
</tr>
<tr>
<td><strong>Subjects:</strong></td>
<td>All registered students 17 to 18 years of age attending the second grade in the senior high schools in the municipality of Falun, N=756</td>
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<tr>
<td><strong>Data:</strong></td>
<td>Retrospective</td>
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<tr>
<td><strong>Design:</strong></td>
<td>Experimental: randomised, controlled clinical trial with a waiting-list control group design</td>
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<tr>
<td><strong>Subjects:</strong></td>
<td>50 subjects (40 women, 10 men) from Study I with SAD or S-SAD</td>
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<tr>
<td><strong>Setting:</strong></td>
<td>The four light therapy rooms at the Sleep Clinic Avesta Hospital, Gagnefs Primary Health Care Center, Falun Psychiatric Outpatient Clinic and Säters Psychiatric Clinic</td>
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<tr>
<td><strong>Data:</strong></td>
<td>Prospective; assessments the week before treatment, at post-treatment and at the one month follow-up</td>
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<th>Study IV (2002-2004)</th>
<th>Aims: (i) evaluate treatment effects of bright light on fatigue, sleepiness and health-related quality of life in persons with SAD and S-SAD and (ii) explore and validate empirically derived subgroups in the sample and evaluate differential treatment effects in the subgroups</th>
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<td>Descriptive and comparative</td>
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<tr>
<td><strong>Setting:</strong></td>
<td>Same as in Study III</td>
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<tr>
<td><strong>Data:</strong></td>
<td>Same as in Study III</td>
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*Figure 3. Overview of the design in the four studies in the thesis.*
Subjects, procedure and design

Study I concerns prevalence of winter depressive mood in a general population sample and Study II prevalence among adolescents in a municipality. Study III and IV concern treatment effects of bright light and an analysis of subgroups in the sample.

**Study I**

To estimate prevalence of winter depressive mood among adults, a self-report questionnaire was sent to a proportionally stratified random sample from the general population consisting of 2500 persons between 18 and 65 years of age, living in five municipalities in Dalarna. The questionnaire together with an invitation to participate, written information about the study and a return envelope were sent to the sample during the first week of December 2001. The first reminders were mailed in the middle of January 2002 and the second in the middle of February. The questionnaires were answered confidentially. The response rate was 66.3% (1657/2500) and was higher for women (72.2%) than for men (60.6%). Thus, the sample consisted of a slightly larger percentage of women compared to the population from which the sample was drawn (sample: 53.3% women and 46.7% men; population: 50.9% women and 49.1% men). The response rate was particularly low among young men ≤ 24 years of age (40.3%).

In order to estimate prevalence figures among those not responding, we selected a random sample of 182 non-responders using a table of random digits (n=182/843, 22 %). We were able to contact 82 of these by telephone and a total of 77 provided a short version of the questionnaire while 5 refused (77/843, 9.1 %). Few of the interviewed non-responders experienced any seasonal symptoms. None had scores equivalent to “SAD” and only three (3/77) had scores equivalent to “S-SAD”.

**Study II**

To estimate prevalence of winter depressive mood among adolescents, a self-report questionnaire was distributed to all registered students 17 to 18 years of age attending the second grade in all the senior high schools in the municipality of Falun (N=866). Permission to conduct the study was obtained from the municipal school director as well as from the principals of each of the four schools. Information about the study (during 30-60 min) was given at regular staff meetings in December 2002 and January 2003. Students and their parents were informed two weeks in advance through a letter distributed to the students by their teachers, together with the instruction to deliver the written information to their parents. Teachers in charge of the second year classes received written information two weeks in advance together with detailed instructions about the procedure. These teachers were responsible for distributing and collecting the questionnaires within a two-
week period at the end of January 2003. All classes but one completed the questionnaires within this time frame. The questionnaire together with the study information and a return envelope were sent to the home address of students registered at school but absent for a longer period (n=11). The questionnaires were completed anonymously.

The response rate was 87.3% (756/866). There was no difference between responder gender distribution and gender distribution in the total group (53.6% girls and 46.4% boys).

**Study III and IV**

Study III evaluates short- and long-term effects on depressed mood following treatment with bright light in a sample of persons with SAD and S-SAD. Study IV deals with treatment effects of bright light therapy (BLT) for fatigue, excessive daytime sleepiness and health-related quality of life in the sample from Study III. Study IV is also an analysis of subgroups in the sample from Study III and of differential treatment effects in the subgroups.

The inclusion criteria were: (1) a history of major depressive disorder with a winter seasonal pattern as defined by the DSM-IV (2) or a history of depressive mood during the winter season according to the description of S-SAD by Kasper et al (16), (2) being able to schedule 2-4 hours each morning for ten subsequent working-days and (3) sufficient knowledge of the Swedish language. Exclusion criteria were: (1) clinically judged severe psychiatric or somatic disease, (2) anti-depressive medication, self-medication with the herb St. John’s Wort or treatment with antibiotics (3) pregnancy, (4) an eye condition that precluded the exposure to strong light, (5) current shift work or (6) previous treatment with light therapy.

The recruitment procedure is illustrated in Figure 4. Eligible were all subjects who scored above the cut-off for “SAD” and “S-SAD” on the questionnaire used in Study I (step 1, Figure 4). These persons (N=312/1657) were interviewed by telephone in the spring by the first author (step 2). A total of 221/312 could not be contacted, declined participation or were excluded during the telephone interviews. The remaining 91 subjects were subsequently examined and diagnosed by an experienced psychiatrist in a clinical face-to-face interview, which was performed before subjects were actually experiencing any seasonal symptoms (step 3, Figure 4). Written, informed consent was obtained from the participants during the psychiatrist interview. As a result of the clinical examination another 9 subjects were excluded. The remaining 82 subjects were then asked to contact the first author as seasonal symptoms appeared during the following fall-winter period. Twelve of the 82 subjects did not experience any seasonal symptoms during the study period, 13 could not participate due to recent personal circumstances and 6 were excluded due to new medical problems. A total of 51 subjects were included in the final sample and randomised to either bright light therapy (BLT) or the waiting-list control condition (WLC) followed by BLT. One
subject was excluded shortly after randomisation due to pregnancy and the sample thus consisted of 50 subjects.

Figure 4. Flow chart of subjects’ progression from Study I to Study III and Study IV. The SPAQ refers to the Seasonal Pattern Assessment Questionnaire, which is described in more detail in the measures section.

An illustration of the points in time for the measurements in the experimental and control group is presented in Figure 5. Baseline data were collected before the randomisation. The second baseline in the waiting-list control group was performed three weeks after the first baseline, corresponding to the post-treatment assessment of the experimental group. The questionnaires together with a prepaid return envelope were sent by mail to the subjects’ home address (or, occasionally, handed out personally). The post-treatment assessment was completed during the week after treatment and the follow-up was completed one month after treatment. In total, the experimental group was assessed three times and the control group four times.
Points in time for measurements in study III and IV

<table>
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<tr>
<th>Experimental group</th>
<th>M1</th>
<th>X</th>
<th>X</th>
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<th>–</th>
<th>–</th>
<th>–</th>
<th>M3</th>
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<tr>
<td>Control group</td>
<td>M4</td>
<td>–</td>
<td>–</td>
<td>M5</td>
<td>X</td>
<td>X</td>
<td>M6</td>
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Week 1

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<tr>
<th>M</th>
<th>= measurements</th>
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<tr>
<td>X</td>
<td>= bright light therapy</td>
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<tr>
<td>–</td>
<td>= waiting period/follow-up period</td>
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Figure 5. An illustration of the points in time for measurements in Study III and Study IV. In the experimental analysis in Study III, the differences between the experimental group (N=24) before and after the intervention (MI and M2) were compared to the first and second baseline (M4 and M5) in the control group (N=24). In the follow-up analysis in Study III and IV, the scores for the merged groups (N=47) before treatment (M1 and M5), after treatment (M2 and M6) and at the one-month follow-up (M3 and M7) were compared.

Randomisation (Study III)

When a subject entered the study and after baseline scorings were returned, an e-mail was sent to the statistical advisor in the project, who was situated in a nearby town. He was responsible for the randomisation procedure which was performed with a computer. Sequence was blind to the experimenter until the intervention was to be carried out. Restricted randomisation with a probability factor of 0.8 in favour of the group that would minimize imbalance in number of participants between groups was used (128). This procedure was preferred, since there is a greater risk for imbalance between groups with simple randomisation in small to moderate sized group. The method is also suitable for trials when subjects enter one at a time in the study. To ensure equal gender distribution in groups, randomisation was performed in separate lists for men and for women (116).

Power analysis (Study III)

A sample size of 24 subjects per group was estimated on the basis of a power analysis where 50 percent of the subjects in the experimental group were predicted to achieve a 50% reduction of depression scores (the total score on the 29-item SIGH-SAD/SR) with a corresponding proportion of 10 percent with a similar reduction in the control group. An 80 percent chance to detect a significant difference and a two-tailed p-value of 0.05 was used.
The intervention (Study III and Study IV)

The BLT setting included four separate light rooms which all had white painted walls and light-coloured furniture. Patients sat comfortably in small groups reading, talking or just relaxing. The light source was fluorescent tubes with full-spectrum light in the ceiling and on the walls. Treatments were given between 06.00 and 09.00 a.m., for 1.5 to 2 h daily on ten consecutive weekdays. The interventions were carried out for two consecutive winter seasons (2002-2003 and 2003-2004) during the period October through February at four different locations (Avesta, Falun, Gagnef, Säter). The maximum travelling distance for patients to treatment facilities was approximately 30 kilometres and subjects could choose the most convenient location for treatment. The only financial compensation offered was for travel expenses.

Light intensities (lux and candela/m²) were measured by a safety engineer twice a year in September and March at several fixed locations and directions. The measurement of light intensity “horizontally as the eyes see” (sitting in chairs) was considered the most appropriate value to report and was approximately 1100 lux (Gagnef), 1900 lux (Avesta), 2200 lux (Falun) and 4300 lux (Säter). Even though there were differences in light intensity between the four light therapy rooms, the light intensity in each room was stable during the study period.

Attrition (Study III and Study IV)

Two persons were excluded or declined participation after randomization; one excluded due to pregnancy in the experimental group (before baseline assessments) and the other declined participation after 2nd baseline in the control group. Another person was lost to 2nd baseline assessments (a crossover; no waiting-period due to personal circumstances). In addition, due to a severe cold, one person in the experimental group was lost to post-treatment assessment.

The few single missing items in the SIGH-SAD/SR (<0.5%) were imputed using the method of last value carried forward or with 0 if missing at baseline (129). The few single missing items in the SF-36 (<0.5%) were imputed according to the instructions in the Swedish manual (130). For VAS-ratings a minimum of 5/7 daily ratings were considered sufficient and, with those criteria, there were no single missing items in the VAS, the ESS or the FQ. A modified intention-to-treat analysis was used; all persons were analyzed in the group to which they were randomised, but, when persons or entire assessments were lacking, these data were not imputed.

Baseline characteristics in the experimental and control group (Study III)

There were no statistically significant differences between the two groups at baseline regarding demographic variables, treatment expectations or any of
the measures used. However, it was decided that the slightly higher but non-significant depression score in the control-group might influence results and, therefore, differences between the experimental and control group were analysed with one-way ANCOVAs and the baseline 29-item SIGH-SAD/SR total score as a covariate.

**General information on cluster analysis (Study IV)**

Cluster analysis is a person-oriented, multivariate statistics method that has been used in psychiatric and other research to create empirically based classification of clinical syndromes or generate hypotheses through data exploration (131, 132). There are a variety of cluster methods that can generate different types of solutions, but the basic procedure in most methods comprises the same five steps; the selection of the sample and cluster variables, the computation of similarities (a correlation or a distance measure), the use of a cluster method to create groups and validation of the results. If variables have different scales, they are generally (but not always) transformed into standardized scales before computations. One of the most commonly used similarity measures is the hierarchical agglomerative cluster method (in this case Ward’s, which is recommended for small samples like ours) (132).

Since cluster analysis always results in clusters, there is a need for a validation procedure to evaluate whether clusters are valid, useful or meaningful to the clinician. Generally, significance testing on independent variables (not used in the formation of the clusters) and over time are two of the most recommended validation methods (132). Both methods were used in Study IV.
Measures

An overview of the measures and statistical analyses used in the four studies is presented in Table 1.

Table 1. Overview of measures and statistical analyses in the four studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Measure</th>
<th>Statistical analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>I and II</td>
<td>Seasonal Pattern Assessment Questionnaire (SPAQ)(17) (Study I), Kiddie-SPAQ (K-SPAQ)(34) (Study II)</td>
<td>Chi-square test/Fischers’ exact test, Mann-Whitney U-test/Kruskal-Wallis test, Student’s t-test/ANOVA, Reliability analysis (Cronbach’s alpha), Factor analysis, Multiple logistic regression (Study I)</td>
</tr>
<tr>
<td>III</td>
<td>The structured Interview Guide for the Hamilton Depression Rating Scale –29 item Seasonal affective disorders and self-rating version (SIGH-SAD/SR)(133), Demographic data, Pretreatment expectations(134)</td>
<td>Mann-Whitney U-test, Chi-square test, Student’s t-test, ANCOVA, Repeated measures ANOVA with Bonferroni post hoc test, Multiple linear regression analysis</td>
</tr>
<tr>
<td>IV</td>
<td>SIGH-SAD/SR(133), Fatigue Questionnaire (FQ)(84), Epworth Sleepiness Scale (ESS)(135), The Swedish Short Form –36 Health Survey (SF-36)(130), Visual Analogue Scales (VAS) of mood and sleepiness</td>
<td>Pearson correlation coefficients, ANOVA, Repeated measures ANOVA with Bonferroni post hoc test, Ward’s hierarchical agglomerative cluster analysis with a Euclidian distance measure, Chi-square test/Fischer’s Exact Test, Kruskal-Wallis test</td>
</tr>
</tbody>
</table>

Seasonal symptoms

Study I

The Seasonal Pattern Assessment Questionnaire (SPAQ), is an extensively used, retrospective, self-report questionnaire including 33 items concerned with seasonal and weather symptoms and some additional items on background information (17, 22). The most widely used part of the SPAQ is the Global Seasonal Score (GS-score), a sum score of six items asking about degree of seasonal changes in energy level, mood, sleep length, social activity, weight and appetite. These items are scored on a five-graded Likert scale ranging from 0 (“no change”) to 4 (“extremely marked change”). The total score varies from 0 to 24. The classification of subjects into “SAD” or “S-SAD” were based on the commonly used criteria by Kasper et al (17, 23). The cut-off for “winter SAD” was a GS-score >11 in combination with the severity of the seasonal problem being “marked”, “severe” or “disabling” and the month(s) feeling the worst. The criteria for “winter S-SAD” was a GS-score of 9 or 10 in combination with seasonal problems being at least a
“mild problem” or a GS-score of 11 or more in combination with seasonal problems being mild or moderate and the month(s) “feeling the worst”.

Psychometric studies of the SPAQ mainly involve only the GS-score items. In the present study, reliability testing showed that the internal consistency was adequate (Cronbach’s alpha 0.88) and factor analysis resulted in one factor. Test-retest reliability generally varies between 0.65 – 0.87 in different studies (25). Sensitivity was high (94%) while specificity was low (73%) (136) which is different to results from another study in which sensitivity was low (44%) and specificity high (94%) (137). The SPAQ GS-score differentiated between groups of subjects with SAD, bipolar affective disorder and healthy controls (138) and between patients with seasonal depression, nonseasonal depression, bipolar disorder and healthy controls (139).

Study II
A child and adolescent version of the SPAQ, the K-SPAQ, was introduced by Swedo and co-workers (34). The K-SPAQ includes 29 seasonal items and some additional items concerned with clinical and background information. This version was chosen for the adolescent sample in our study mainly because language and questions were adapted to young persons, in which seasonal symptoms may present in a slightly different way than for adults (140) and because it includes items concerned with the school situation. Answers to the ten items in the GS-score (these are six in the SPAQ) are scored on a five-graded Likert scale ranging from 0 (“no change”) to 4 (“extremely marked change”). The total score varies from 0 to 40. The cut-off for winter depressive mood was a GS-score >18, in combination with the question about seasonal symptoms being a “pretty bad problem”, “very bad problem” or “extremely bad problem” and the month(s) “feeling the worst” or “having the least energy” (34). To make it possible to rank subjects according to the severity of seasonal symptoms, those scoring above the cut-off were further divided into three subgroups according to the GS-score; mild symptoms (18-23 p), moderate (24-29) and severe (30-40) (the division based on the authors clinical experience).

In the present study, the internal consistency reliability of the GS-score was adequate (Cronbach’s alpha 0.87) and factor analysis revealed a two-factor structure. To our knowledge, there were no previous studies of the reliability or validity of the K-SPAQ. The K-SPAQ was translated into Swedish by the first author in collaboration with a professional translator.

Pretreatment expectations
Study III
Pre-treatment expectations were measured by four items originally presented by Borkovec and Nau (134), each item scored from 1 (low) to 10 (high). Since results on these four items were similar between groups, only results
for the two items judged to be the most central to the study were used. These two items concerned “logical consistency” and “confidence in treatment success”, while the two omitted items dealt with confidence in recommending the treatment to others with similar or related disorders.

**Depressed mood**

*Study III and IV*

The Structured Interview Guide for the Hamilton Depression Rating Scale – Seasonal Affective Disorders self-rating version (SIGH-SAD/SR) is an extended version of the 21-item version of The Hamilton Depression Rating Scale (HDRS or HAM-D) (141), supplemented with 8 items specific for SAD patients’ atypical symptoms (24, 133). The SIGH-SAD or the self-rating version of the SIGH-SAD (the SIGH-SAD/SR), are commonly used measures in clinical trials of SAD (18, 61, 142). The latter was the primary outcome measure used in the present study. A previous Swedish version of the SIGH-SAD/SR was revised by the first author and then back translated into English by a professional translator. The two versions showed few discrepancies.

A review of the psychometric properties of the HDRS have been published (143). The internal consistency reliability of the HDRS was considered adequate (Cronbach’s alpha ranging from 0.46 to 0.97). Tests of the convergent validity show that the HDRS correlates well (i.e. Pearson $r >0.5$) with most other depression scales. Factor analysis showed that HDRS consisted of several dimensions with the number of factors ranging between two to eight (143). To my knowledge, corresponding studies on the psychometric properties of the SIGH-SAD/SR have not been published.

Daily global ratings of mood on a bivariate Visual Analogue Scale (VAS) were performed for one week at each assessment (Study IV). Subjects were instructed to put a mark on a 100mm vertical line with end-point values only (very sad – very happy) according to the present situation. The mean value from each week was used in the analysis.

**Fatigue**

*Study IV*

The Fatigue Questionnaire (FQ) was developed in Norway for clinical and epidemiological purposes (84). It includes two subscales, physical fatigue and mental fatigue, but only the total score was used in the present study. The eleven items concern fatigue experienced during the last month (changed to last week in this study) and are scored on a four-graded Likert scale ranging from 0 (“less than usual”) to 1 (“not more than usual”), 2 (“more than usual”) and 3 (“much more than usual”). The total score varies from 0 to 33. Norms for the general population have been published (84) as well as scores for patients with different diagnoses (144). The FQ was shown
to be correlated to two other measures of fatigue (Pearson \( r \) ranging between 0.28 and 0.46) (80) and the internal consistency reliability was high (Cronbach’s alpha 0.89) (145).

**Daytime sleepiness**

*Study IV*

The Epworth Sleepiness Scale (ESS) is a questionnaire commonly used in sleep medicine to measure persistent day-time sleepiness (135, 146). The eight items concern situations in which the risk of falling asleep or “dozing off” is estimated and answers are scored on a four-graded Likert scale ranging from 0 (“would never doze”) to 3 (“high chance of dozing”). The total score varies from 0 to 24. A total score \( \leq 8 \) is considered to be within the normal range and a score \( \geq 10 \) is commonly used as an indication of excessive daytime sleepiness (135). Psychometric studies have shown high internal consistency (Cronbach’s alpha 0.88), an adequate test-retest reliability (Pearson \( r = 0.82 \)) and factor analyses have resulted in one factor (146). The ESS discriminated between several patients groups with sleep disorders and normal controls (135, 146). Even though there is some debate about what underlying construct the ESS actually measures – sleepiness, sleep propensity or some other construct – it is correlated to clinical outcomes such as traffic accidents (147).

A bivariate Visual Analogue Scale (VAS) for sleepiness (very sleepy – very alert) was filled in for one week according to the procedure described above for depressed mood.

**Health-related quality of life**

*Study IV*

The SF-36 is a well-known measure of health-related quality of life in the population (130) and in this study the seven-days’ version was used. The thirty-six items are summed up in eight domains/subscales, of which the first four constitute the summary measure physical health (PCS) and the last four the summary measure mental health (MCS). One of the subscales in the MCS is the Vitality (VT) scale, which measures feelings of being tired or worn-out as opposed to alert and energetic. Norms for the Swedish population and different subgroups are available (130). The mean value in the general population for the PCS and MCS summary scales is set at 50.0 (SD for the PCS 9.7 and the MCS 10.3) (130). There are a number of studies on the psychometric properties of the SF-36 and for example, the questionnaire differentiated well between groups of patients and internal consistency reliability was considered sufficient (Cronbach’s alpha >0.7) (130, 148). Factor analysis supported the two-dimensional structure (130, 148, 149).
Data analyses

An overview of the statistical analyses is presented in Table 1 (on a previous page).

Study I and II

Group differences for categorical variables were analyzed with the Mann-Whitney U-test (ordinal data, two groups), the Kruskal-Wallis test (ordinal data, three or more groups), Chi Square tests (nominal data, two or more groups) or Fischer’s Exact Test (when expected values for the number of cases/cells were < 5). Group differences for continuous variables were analyzed with the Student’s t-test or analysis of variance (ANOVA) and a subsequent Bonferroni Post Hoc test (if three or more groups). Multiple logistic regression analyses with dichotomized variables were used to calculate odds ratios (Study I). Factor analysis was done with orthogonal varimax rotation. The internal consistency reliability was assessed by the Cronbach’s alpha. A two-tailed p-value of 0.05 was used in the significance testing. Statistical significance was denoted with p<0.05, p<0.01, p<0.001 and n.s. (not significant). The SPSS for Windows, version 11.5 was used for all analyses.

Study III

Differences between the two groups at baseline were assessed by the Student’s t-tests (continuous variables), the Mann-Whitney U-tests (ordinal data) and Chi-square tests (nominal data). Differences between the experimental and control group were analysed with one-way ANCOVAs and the 29-item SIGH-SAD/SR total score at baseline as a covariate. Multiple linear regression analysis (Enter method) was performed to obtain an estimate of expected change in absolute number in the SIGH-SAD/SR score. Treatment effects at the one-month follow-up for the merged group (N=47) were estimated with one-way repeated measure ANOVAs and subsequent Bonferroni Post Hoc tests. When Mauchle’s test of sphericity was significant, a Greenhouse-Geisser correction of degrees of freedom was used (150). A two-tailed p-value of 0.05 was used. Statistical significance was denoted with p<0.05, p<0.01, p<0.001 and n.s. (not significant). All analyses were performed in SPSS, version 15.

Study IV

Treatment effects for the total group (N=47) were analyzed with one-way repeated measures ANOVAs and subsequent Bonferroni Post Hoc tests. When Mauchle’s test of sphericity was significant, a Greenhouse-Geisser correction of degrees of freedom was used (150).

When considering what variables to include in the cluster analysis, the relations between the measures were calculated in order to evaluate whether correlations between them were within an acceptable range. If variables are
highly correlated (Pearson $r >0.7$), they may be considered measures of the same construct with a resulting implicit weighting of variables (132). Results showed that the correlations generally were acceptable and of moderate strength (Table 2). The ESS had a low or non-existent correlation to the other measures, while the FQ was related to all the other measures. Unexpectedly, the VAS sleepiness scale was not related to the ESS. Both VAS scales had moderate strong correlations to each other and to the SF-36 MCS.

Table 2. Correlation coefficients (Pearson $r$) for the measures used in Study IV, the two subscales in the SIGH-SAD/SR (HAMD-21 and Atyp-8), the Epworth Sleepiness Scale (ESS), the Fatigue Questionnaire (FQ), two VAS-scales and the SF-36 summary measures physical health (PCS) and mental health (MCS).

<table>
<thead>
<tr>
<th>Measure</th>
<th>HAMD-21</th>
<th>Atyp-8</th>
<th>ESS</th>
<th>FQ</th>
<th>VAS Mood</th>
<th>VAS Sleepiness</th>
<th>SF-36 PCS</th>
<th>SF-36 MCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAMD-21</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Atyp-8</td>
<td>0.5*</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ESS</td>
<td>0.0</td>
<td>0.0</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FQ</td>
<td>0.5*</td>
<td>0.5*</td>
<td>0.2</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VAS Mood</td>
<td>0.4*</td>
<td>0.2</td>
<td>0.1</td>
<td>0.3*</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VAS Sleepiness</td>
<td>0.3*</td>
<td>0.4*</td>
<td>0.0</td>
<td>0.4*</td>
<td>0.6*</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>0.5*</td>
<td>0.3</td>
<td>0.1</td>
<td>0.4*</td>
<td>0.3*</td>
<td>0.2</td>
<td>1.0</td>
<td>-</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>0.6*</td>
<td>0.4*</td>
<td>0.1</td>
<td>0.6*</td>
<td>0.6*</td>
<td>0.6*</td>
<td>0.1</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*p-value <0.05

The cluster analysis was performed with Ward’s method which is a hierarchical agglomerative method optimizing the minimum variance within clusters. The squared Euclidian distance was used as the similarity measure (132). The variables used in the cluster analysis were baseline data from the two subscales in the SIGH-SAD/SR (the HAMD-21 and Atyp-8), the FQ and the ESS. Before performing the cluster analysis, the scores were transformed into z-scores. Differences between clusters at baseline were analyzed with one-way ANOVAs. Validation of clusters on demographic variables was performed with Chi-square tests (nominal data), Kruskal-Wallis tests (ordinal data) and Fischer’s tests (when expected values for number of cases/cells were <5). Group x time interactions were analyzed with repeated measures ANOVAs. A two-tailed p-value of 0.05 was used. Statistical significance was denoted with p<0.05, p<0.01, p<0.001 and n.s. (not significant). All analyses were performed in SPSS, version 15.
Results

Prevalence

The adult sample (Study I)
Prevalence of “winter SAD” was estimated at 8.0% (133/1657) and “winter S-SAD” at 10.8% (179/1657). Depressive mood during the summer was rare (0.3%). A total of 3.1% (52/1657) reported seasonal problems to be severe or disabling and 19.3% (319/1657) that everyday life was negatively affected. Both “winter SAD” and “winter S-SAD” was more frequent among women compared with men (“winter SAD”: women 10.3%; men 5.4%; $\chi^2(1) = 13.35$, $p<0.001$; “winter S-SAD”: women 13.9%; men 7.3%; $\chi^2(1) = 19.02$, $p<0.001$). Prevalence figures decreased with increasing age ($\chi^2(4) = 29.1$, $p<0.001$) and was twice as high in the youngest age group (18–24 years: 28.6%) compared to the oldest (55-64 years: 11.3%).

Although the reported sleep length increased in all groups during the winter compared to the summer, the increase was more pronounced in the (merged) “winter SAD/S-SAD” group compared to the “non-SAD” group (difference in sleep length between winter and summer; “winter SAD/S-SAD”: 82 min; “non-SAD”: 41 min; $t(1598) = 8.6$, $p<0.001$). There was also a larger percentage of the “winter SAD/S-SAD” that reported seasonal weight gain compared to the “non-SAD” group ($\chi^2(6) = 164.9$, $p<0.001$). A larger proportion in the “winter SAD/S-SAD” group compared to the “non-SAD” group reported having consulted a doctor during the previous 2 years due to depression, lack of energy or sleep problems (“winter SAD/S-SAD” 59.9%, “non-SAD” 14.9%; $\chi^2(1) = 180.2$, $p<0.001$).

In summary, slightly less than 20% in this sample of the adult general population, reported that they were affected by winter depressive mood. Prevalence was higher among women and younger persons.

The adolescent sample (Study II)
Among the adolescents, a total of 20.1% (151/751) reported winter depressive mood and prevalence was higher among girls (25.5%) than boys (13.8%) ($\chi^2(1) = 15.8$, $p<0.001$). The majority (90/151) reported what was considered mild symptoms, while 2.4% of the total sample (18/751) were considered to have more severe symptoms. There were no differences in the proportion of girls and boys with mild, moderate or severe symptoms (per-
percentage girls/boys; mild: 56.3/66.7; moderate: 31.1/22.9; severe 12.6/10.4; \( \chi^2(2) = 1.49, \text{n.s.} \). Depressive mood during the summer was rare (0.1%).

The difference in sleep length (median value) between summer and winter was 2 h for adolescents with winter depressive mood compared with 1 h for adolescents with no such problems. There was a larger percentage in the group with winter depressive mood compared to the group without such symptoms, reporting difficulties getting up in the morning during the winter period (percentage of depressive mood/no depressive mood answering “no difference”: 2.7/13.6, “yes, a little more difficult”: 17.4/45.8, “yes, much more difficult”: 79.9/40.6; \( \chi^2(2) = 74.2, p<0.001 \)). There was a larger percentage in the group with winter depressive mood reporting an increase in craving for sweets during the winter period (percentage of depressive mood/no depressive mood answering “no difference”: 34.2/58.0, “yes, a little more”: 36.9/32.4, “yes, much more”: 28.9/9.5; \( \chi^2(2) = 46.7, p<0.001 \)).

There was also a larger percentage in the group with winter depressive mood compared to the group without such symptoms, reporting that they had many times thought about consulting a doctor for their problems (percentage of depressive mood/no depressive mood answering “no”: 30.5/74.9, “yes, occasionally”: 39.7/18.6, “yes, many times”: 29.8/6.5; \( \chi^2(2) = 118.1, p<0.001 \)). The majority (59.3%) reported that seasonal symptoms started between the ages 13 to 15, while a smaller portion (17.3%) reported that these symptoms had started as early as between the ages 7 to 12.

In summary, prevalence of winter depressive mood in the sample of adolescents was approximately 20%. Prevalence was higher in girls than boys. Symptoms reported by adults, such as a pronounced increase in sleep length and craving for sweets, were common in the adolescent sample as well.

**Treatment effects**

**Depressed mood (Study III)**

Between-group ANCOVA showed a significant main effect for the 29-item SIGH-SAD/SR total (depression) score, \( F(1, 45) = 16.7, p<0.001 \) (Table 3). There were similar main effects for the two subscales; the HAMD-21 (typical depressive symptoms subscale), \( F(1, 45) = 11.5, p<0.001 \) and the Atyp-8 (atypical depressive symptoms subscale), \( F(1, 45) = 18.1, p<0.001 \). Mean values and standard deviations are presented in Table 3. Multiple linear regression analysis showed that the expected reduction in total SIGH-SAD/SR score after BLT was estimated to 9.7 (adjusted mean value, 95% CI: 4.9-14.4).

In the bright light therapy (BLT) group a total of 54.2% (N=13/24) improved \( \geq 50\% \) compared to baseline on the 29-item SIGH-SAD/SR total score, while no such improvement was seen in the waiting-list control (WLC) group (N=0).
Table 3. Mean values (SD) for the 29-item total SIGH-SAD/SR depression score and the two subscales (HAMD-21 and Atyp-8) at baseline and post-treatment in the BLT experimental group (N=24) compared to first and second baseline in the WLC waiting-list control group (N=24).

<table>
<thead>
<tr>
<th>Measure: SIGH-SAD/SR</th>
<th>1st baseline</th>
<th>Post-treatment / 2nd baseline</th>
<th>Between-groups ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BLT (Mean (SD))</td>
<td>WLC (Mean (SD))</td>
<td>BLT (Mean (SD))</td>
</tr>
<tr>
<td>Total score</td>
<td>21.8 (10.1)</td>
<td>25.4 (8.1)</td>
<td>24.8 (9.0)</td>
</tr>
<tr>
<td>HAMD-21</td>
<td>14.2 (6.9)</td>
<td>16.2 (5.8)</td>
<td>15.5 (6.4)</td>
</tr>
<tr>
<td>Atyp-8</td>
<td>7.6 (4.1)</td>
<td>9.3 (4.0)</td>
<td>9.4 (3.5)</td>
</tr>
</tbody>
</table>

*p-value <0.001

Repeated measures ANOVA showed a significant reduction over time for the merged group (N=47) on the 29-item total SIGH-SAD/SR (depression) score, F(2, 92) = 80.8, p<0.001 (Table 4). There were similar main effects for the HAMD-21 (typical depressive symptoms) subscale, F(2, 92) = 64.7, p<0.001 and Atyp-8 (atypical depressive symptoms subscale), F(1.7, 78.2) = 49.4, p<0.001. Mean values and standard deviations are presented in Table 4. Post hoc analyses showed a significant difference between baseline and post-treatment for the 29-item SIGH-SAD/SR total score (mean reduction 11.7, 95% CI 8.1-15.2) and there was also a significant difference between post-treatment and follow-up (mean reduction 3.2, 95% CI 0.2-6.2). The proportion improved ≥50% on the 29-item SIGH-SAD/SR total score compared with baseline, was 59.6% at post-treatment and 83.0% at the one-month follow-up.

The proportion with scores on the 29-item SIGH-SAD/SR scale ≤8 (i.e. no depressed mood) (98) was 4.3% at baseline, 55.3% at post-treatment and 63.8% at the one-month follow-up. The proportion with a 29-item total SIGH-SAD/SR score <20 (scores ≥20 indicate possible depression) (142) was 38.3% at baseline compared with 97.9% at the one-month follow-up.

Table 4. Mean values (SD) for the 29-item total SIGH-SAD/SR depression score and the two subscales (HAMD-21 and Atyp-8) for the merged group (N=47) at baseline, post-treatment and the one-month follow-up.

<table>
<thead>
<tr>
<th>Measure: SIGH-SAD/SR</th>
<th>Baseline</th>
<th>Post-treatment</th>
<th>Follow-up</th>
<th>Within-subjects repeated measures ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>F (df)</td>
</tr>
<tr>
<td>Total score</td>
<td>22.6 (9.1)</td>
<td>10.9 (9.1)</td>
<td>7.7 (5.3)</td>
<td>80.8 (2, 92)*</td>
</tr>
<tr>
<td>HAMD-21</td>
<td>14.3 (6.2)</td>
<td>6.7 (5.8)</td>
<td>5.3 (3.7)</td>
<td>64.7 (2, 92)*</td>
</tr>
<tr>
<td>Atyp-8</td>
<td>8.3 (3.9)</td>
<td>3.9 (4.4)</td>
<td>2.4 (2.7)</td>
<td>49.4 (1.7, 78.2)*</td>
</tr>
</tbody>
</table>

*p-value <0.001

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Fatigue, sleepiness and health-related quality of life (Study IV)

Repeated measures ANOVAs showed a significant reduction over time for the FQ (fatigue scale), $F(1.7, 79.4) = 24.7, p<0.001$ and the ESS (sleepiness scale), $F(2, 90) = 59.1, p<0.001$ (Table 5). There was a significant reduction over time for the SF-36 PCS (physical health summary scale), $F(2, 92) = 6.0, p<0.01$ and the SF-36 MCS (mental health summary scale), $F(2, 92) = 66.7, p<0.001$. There were similar reductions over time for the VAS-mood and VAS-sleepiness scales. Mean values and standard deviations are presented in Table 5.

The proportion with a total FQ (fatigue) score below the norms for a general population sample ($FQ < 12$) (84) was 6.4% at baseline compared with 83% at the one-month follow-up. The proportion with scores within the normal range for the ESS (sleepiness) scale ($ESS < 8$) (135) was 27.7% at baseline compared with 84.8% at the one-month follow-up.

Table 5. Mean values (SD) for the Fatigue Questionnaire (FQ), the Epworth Sleepiness Scale (ESS), Visual analogue scales (VAS) and the SF-36 summary measures physical health (PCS) and mental health (MCS) for the merged group (N=47) at baseline, post-treatment and at the one-month follow-up.

<table>
<thead>
<tr>
<th>Measures</th>
<th>Baseline</th>
<th>Post-treatment</th>
<th>Follow-up</th>
<th>Within-subjects repeated measures ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>$F(df)$</td>
</tr>
<tr>
<td>FQ$^1$</td>
<td>19.3 (4.2)</td>
<td>10.7 (7.7)</td>
<td>9.5 (9.8)</td>
<td>24.7 (1.7, 79.4) $^{***}$</td>
</tr>
<tr>
<td>ESS$^1$</td>
<td>10.0 (4.1)</td>
<td>6.4 (4.0)</td>
<td>5.5 (3.1)</td>
<td>59.1 (2, 90) $^{***}$</td>
</tr>
<tr>
<td>VAS$^2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td>49.5 (11.7)</td>
<td>65.5 (15.6)</td>
<td>70.4 (15.1)</td>
<td>57.1 (1.6, 75.8) $^{***}$</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>36.1 (14.9)</td>
<td>60.8 (20.0)</td>
<td>68.5 (14.2)</td>
<td>82.8 (1.7, 77.9) $^{***}$</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS$^3$</td>
<td>47.7 (7.4)</td>
<td>49.0 (6.7)</td>
<td>51.1 (6.6)</td>
<td>6.0 (2, 92) $^{**}$</td>
</tr>
<tr>
<td>MCS$^3$</td>
<td>31.8 (10.4)</td>
<td>46.2 (11.0)</td>
<td>49.8 (8.9)</td>
<td>66.7 (2, 92) $^{***}$</td>
</tr>
</tbody>
</table>

$^{**}$p-value <0.01; $^{***}$p-value <0.001

1 Low values correspond to feeling better. 2 High values correspond to feeling better.
3 The mean value for the general population is set at 50.0 (SD for the PCS 9.7 and MCS 10.3) (130)
Exploring subgroups and treatment effects

Clusters (Study IV)

The result of the cluster analysis is presented in Figure 6. A visual inspection of the dendrogram, based on the size of and relative distance between the clusters, resulted in the choice of a three-cluster solution for further analysis.

Figure 6. The result from the hierarchical agglomerative cluster analysis (Ward’s method) of persons with winter SAD and S-SAD (N=49) presented in a dendrogram. The analysis was based on baseline data from the HAMD-21 and the Atyp-8 (the two subscales in the depression inventory SIGH-SAD/SR), the Fatigue Questionnaire (FQ) and the Epworth Sleepiness Scale (ESS).

Since all three clusters had a high level of fatigue in common, scoring above the population norms for fatigue (FQ≤12.2, SD=4.0) (84), the group as a whole was given the label “Winter fatigue” (Table 6). The subgroups had different levels of depression and sleepiness. On the basis of the similarities
and differences between the subgroups, they were labeled “Mildly depressed-Not sleepy”, “Mildly depressed-Sleepy” and “Depressed-Sleepy”.

Between-groups ANOVA showed a significant main effect for the HAMD-21 (typical depression symptoms subscale), $F(2, 48) = 14.7$, $p<0.001$ and for the Atyp-8 (atypical depression symptoms subscale), $F(2, 48) = 26.3$, $p<0.001$ (Table 6). There were similar main effects for the FQ (fatigue scale), $F(2, 48) = 18.8$, $p<0.001$ and for the ESS (sleepiness scale), $F(2, 48) = 28.7$, $p<0.001$. Mean values for the three clusters and the four cluster variables are presented in Table 6.

Table 6. Mean values (SD) for the variables used in the cluster analysis; the HAMD-21 and Atyp-8 depression subscales, the Fatigue Questionnaire (FQ) and the Epworth Sleepiness Scale (ESS) in the three clusters (baseline data).

<table>
<thead>
<tr>
<th>Cluster variables</th>
<th>Mildly depressed/Not sleepy</th>
<th>Mildly depressed/Sleepy</th>
<th>Depressed/Sleepy</th>
<th>Between-groups ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAMD-21 (SD)</td>
<td>12.9 (4.1)</td>
<td>11.4 (5.0)</td>
<td>20.4 (6.2)</td>
<td>14.7*</td>
</tr>
<tr>
<td>Atyp-8 (SD)</td>
<td>6.9 (2.8)</td>
<td>6.3 (2.7)</td>
<td>12.3 (2.6)</td>
<td>26.3*</td>
</tr>
<tr>
<td>FQ (SD)</td>
<td>16.9 (2.1)</td>
<td>17.7 (4.2)</td>
<td>23.4 (1.8)</td>
<td>18.8*</td>
</tr>
<tr>
<td>ESS (SD)</td>
<td>3.8 (2.2)</td>
<td>11.7 (3.1)</td>
<td>11.5 (2.5)</td>
<td>28.7*</td>
</tr>
</tbody>
</table>

*p-value <0.001

Validation of clusters and treatment effects (Study IV)

There were no statistically significant differences between the clusters on the variables age, sex, civil status, education, duration of seasonal symptoms, comorbid disorders or medication. However, there was a difference for the dichotomous variable working fulltime/part-time/studying vs. not working/being sick-listed (Fisher’s Exact Test = 0.047). Since the majority (44/49) were at work/studying, it was reasonable to assume that this difference did not have any major impact on the interpretation of the results.

Between-groups ANOVA showed that there were significant main effects in the SF-36 PCS (physical health summary measure), $F(2, 48) = 15.2$, $p<0.001$ and the SF-36 MCS (mental health summary measure), $F(2, 48) = 6.1$, $p<0.01$ (Table 7). There were similar main effects for the VAS sleepiness scale, $F(2, 48) = 5.4$, $p<0.01$ and the SPAQ GS-score, $F(2, 48) = 10.1$, $p<0.001$. However, there was not a significant effect on the VAS mood scale, $F(2, 48) = 2.4$, n.s. Mean values and standard deviations are presented in Table 7. Thus, with one exception (the VAS mood scale) the clusters were considered to be valid on the basis of an analysis of background variables and independent measures at baseline.
Table 7. Validation of the three clusters on independent measures (i.e. not used in the cluster analysis). Mean values (SD) for the SF-36 summary measure physical health (PCS) and mental health (MCS), the VAS mood, VAS sleepiness and the Seasonal Pattern Assessment Questionnaire (SPAQ) GS-score (baseline data).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Winter Fatigue</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>F(2, 48)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mildly depressed/ Not sleepy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td>48.8 (4.2)</td>
<td>51.3 (6.3)</td>
<td>40.5 (6.9)</td>
<td>15.2***</td>
</tr>
<tr>
<td>PCS¹</td>
<td></td>
<td>33.1 (11.9)</td>
<td>35.3 (9.2)</td>
<td>24.7 (8.8)</td>
<td>6.1**</td>
</tr>
<tr>
<td>MCS¹</td>
<td></td>
<td>53.3 (16.8)</td>
<td>50.1 (11.2)</td>
<td>43.3 (11.3)</td>
<td>2.4 (n.s)</td>
</tr>
<tr>
<td>VAS²</td>
<td></td>
<td>45.2 (16.5)</td>
<td>37.6 (12.4)</td>
<td>27.7 (13.8)</td>
<td>5.4**</td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td>12.5 (2.9)</td>
<td>11.8 (2.2)</td>
<td>15.5 (2.9)</td>
<td>10.1***</td>
</tr>
<tr>
<td>Sleepiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPAQ GS-score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ The mean value for the general population is set at 50.0 (SD for the PCS 9.7 and MCS 10.3) (130).
² High values correspond to feeling better

There were significant group x time interactions for the ESS (sleepiness scale), F(4, 86) = 5.3, p<0.01 and the 29-item SIGH-SAD/SR total (depression) score, F(3.4, 74.3) = 6.2, p<0.001. There were no such group x time interactions for the FQ (fatigue scale), F(3.5, 76.8) = 1.9, n.s., and, in a similar way, not for the SF-36 PCS (physical health summary measure), F(4, 88) = 2.3, n.s. or the SF-36 MCS (mental health summary measure), F(4, 88) = 1.5, n.s. Furthermore, there were no group x time interactions for the VAS mood scale F(3.3, 72.4) = 0.3, n.s. and not for the VAS sleepiness scale F(3.1, 68.4) = 0.3, n.s. The median values for each cluster at baseline, post-treatment and at the one-month follow-up for the ESS, the FQ, the 29-item SIGH-SAD/SR total score, the SF-36 PCS and SF-36 MCS are presented in box-plots (Figure 7).
Figure 7. Median values for each of the three clusters (subgroups) over time presented as box-plots. The different colours represent baseline (yellow), post-treatment (blue) and the one-month follow-up (green). A reference (horizontal lines) is given for each measure; the Fatigue Questionnaire (FQ) a general population mean set at 12.2 (84); the Epworth Sleepiness Scale (ESS) a commonly used cut-off for excessive daytime sleepiness set at >10 (135). Two reference lines are given for the 29-item SIGH-SAD/SR depression scale, one representing scores for individuals without depressive symptoms set at ≤8 (98) and the other for possible depression set at ≥20 (142). The reference lines given for the SF-36 PCS and MCS represent a mean value for the general population set at 50 (130).
Discussion

General discussion

Prevalence

Prevalence of winter depressive mood was approximately 20% in both the adult and adolescent samples of this project. There is only one other (published) Swedish epidemiological study. In that study, which was performed in Umeå (lat. 64°N), figures of “winter SAD” and “winter S-SAD” were lower (2.2% and 5.7% respectively) compared to our results (8.0% and 10.8% respectively) from Dalarna (around lat. 60°N) (151). In contrast, the proportion experiencing seasonal symptoms as a moderate, marked, severe or disabling problem in that study was 18.9% compared with 15.1% in our study. The difference in prevalence figures between studies may be related to the different age groups included. The study from Umeå included the age groups between 35 and 85 years of age, while in our study the age group ranged between 18 and 65 years of age. In an overview, Eagles reported that prevalence figures were lower among older compared with younger adults (30).

In comparison with other studies with a fairly similar procedure (i.e. use of the SPAQ in general population samples, community-based or primary health care samples from the western world), there are studies presenting both lower and higher prevalence figures. For example, among Icelanders, the prevalence rate for “SAD and S-SAD” was lower (varying from 5% to 11%) (152, 153) while in a study conducted in Alaska, prevalence was higher (approximately 28%) compared to our study (18.8%) (29).

The prevalence rate of winter depressive mood among adolescents in our study (20.1%) is much higher compared to the study by Swedo et al (5.5% in a similar age group) (34). However, our results correspond well to several other studies in young adults. Even though results from the K-SPAQ and the SPAQ are not directly comparable, there are striking similarities between results from our study (girls 25.5% and boys 13.8%) and a study from Scotland performed in a primary health care and community sample and presenting figures separately for young adults between the ages 16 to 24 (girls 25.1% and boys 13.4%) (30).

In a recent study from Italy (154) seasonality (the SPAQ GS-score) was significantly associated with age and gender in children between 10 and 17 years of age. In that study, the percentage with “SAD” and “S-SAD” among
10 to 13 year olds varied between 5% and 10% and without any gender differences. From the age of 15, the prevalence rate increased and the increase was larger for girls than for boys. Results from our study and the few other cross-sectional studies in children and adolescents, support the hypothesis that winter depressive mood exists among children, increases during puberty and is as high among post-pubertal adolescents as it is in young adults (35, 36). The character of the symptoms reported by the adolescents in our study was similar to that reported by adults. For example, a more pronounced increase in sleep length during the winter season, problems with daily rhythms (difficulties getting up in the morning) and stronger craving for sweets during the winter period.

Recently, high seasonality scores were associated with other types of self-reports of mental health problems, such as sleep problems (difficulties falling asleep, staying asleep or early morning awakenings) and excessive daytime sleepiness (155), depression and anxiety (156). Other recent studies showed that high seasonality scores predicted low levels of health-related quality of life (157), were associated with a higher dissatisfaction with eating (158) and was a risk factor of metabolic syndrome, even after controlling for a number of previously known risk factors (159).

To summarize, there are some results that appear to be rather consistent across samples and studies from the western world, including the results from our studies. First, the existence of winter depressive mood per se, seems to be a robust and stable finding, even though the numbers vary between studies. Second, the higher prevalence among women compared with men is a fairly consistent finding. Third, there seem to be an increase in prevalence rates beginning at puberty, with a peak in young adults or middle-aged adults, followed by a decrease in prevalence from approximately the age of 45 to 50.

**Treatment effects**

**Depressive mood**

The main finding in the clinical treatment study was that depressive mood was reduced in persons with winter SAD and S-SAD following treatment with bright light therapy (BLT) and that these positive results were maintained for at least one month. Both the typical depressive symptoms and the atypical depressive symptoms subscales were improved. To our knowledge, this was the first study evaluating BLT in SAD and S-SAD with a waiting-list control group design. The waiting period of three weeks and the follow-up period of one month was a compromise, considering time limits in relation to the winter season and the individual onset and remission of symptoms.

There are large differences between BLT studies in designs, measures and samples, which makes it difficult to compare the results directly. One option
is to compare clinical response measures (for example the percentage improved ≥50%). One of the few other studies performed in a light room is the 1995 Swedish study by Thalén et al, which had an open design and included 68 patients with seasonal depression and another 22 patients with nonseasonal depression (6). In that study, 53% of the patients with SAD improved ≥50%, which is similar to our results (54%). In a controlled study including 96 patients with SAD, bright light therapy (light boxes) and pharmacological treatment were equally effective; 67% of both groups improved ≥50% (61). Another recent study comparing five different treatment regimens in a randomised parallel-group design including 99 patients with SAD, showed that the percentage that improved ≥50% following BLT was 57% (160).

There are few clinical studies of BLT in S-SAD. Results from the open study by Levitt and co-workers (19), showed that there was a larger proportion with SAD (69%) than S-SAD (40%) that improved ≥50% (in combination with a total score on the 29-item SIGH-SAD/SR ≤14). Contrary to this, Lam and co-workers (18) in a retrospective study, found that there was a larger proportion with S-SAD (78%) than SAD (66%) that improved ≥50% following BLT.

Light and behaviour

It is obvious that persons with winter fatigue and winter depression are not primarily lacking treatment with BLT, rather sufficient amounts of bright daylight. We do not know what levels of illumination humans need to achieve optimal mental and physical health (161) but one of the most obvious variables affecting human light exposure is behaviour – whether we stay indoors or go outside during daylight.

In a prospective study of exposure to outdoor and indoor levels of illumination in healthy people, results indicated that both seasons and geographic location strongly influenced human illumination exposure (161). For example, from summer to winter, subjects in Michigan, USA showed a 22-fold reduction in time spent in light intensities of >10000 lux (about the same as the light on a clear day without direct sunshine). In a naturalistic study of ambient light, mood and social behaviour in mildly seasonal subjects, exposure to light >1000 lux averaged 26.0 min per day in winter and 91.2 min in summer (162). The authors concluded that the participants most likely had insufficient bright light exposure to obtain optimal mood for most of the days in winter and for some of the days in summer.

A previous study showed that persons with SAD compared to healthy controls, spent much more time outdoors during the summer but there were no differences between groups during the winter (163). When expressed in percentages of the summer outdoor values, persons with SAD received even less daylight in winter; only 40% compared to 67% for controls. In a prospective study from Canada, healthy subjects with S-SAD kept daily recordings of mood and social interactions, while at the same time wearing a
wrist device measuring both motor activity and light intensity (162). The results showed that regardless of season above average exposure to bright light (>1000 lux) was associated with better mood, less quarrelsome and more agreeable behaviours.

**Health-related quality of life, sleepiness and fatigue**

HRQoL was impaired in the sample at baseline. The score for the mental health summary scale (MCS) in the SF-36 was markedly low compared to Swedish normative data (130). The degree of impairment is similar to those reported in other studies in both seasonal and nonseasonal depression (78, 164, 165). Results for the MCS scale at baseline in our study (mean value 31.8, SD 10.4) is below a proposed cut-off on the SF-36 MCS indicating possible depression (mean value ≤42) (166). In one of the studies of SAD patients, HRQoL was markedly low during the winter and then significantly improved and within the normal range during the summer (77). Results from the present study showed in a similar way, that both the mental (MCS) and physical (PCS) health measures in the SF-36 improved and were close to population norms at the one-month follow-up (130).

In nonseasonal depression, it is well known that sleep may be impaired and excessive daytime sleepiness increased (167). Results from a study in the general population showed that depression was a risk factor for excessive daytime sleepiness (168). In another study of patients with nonseasonal depression, half of the patients experienced excessive daytime sleepiness but on average to a moderate degree (169). The latter corresponds to results from our study, where level of excessive daytime sleepiness was moderately high in the sample at baseline. The mean value for the Epworth Sleepiness Scale (ESS) (at baseline) in our study was 10.0 (SD=4.1), which is higher compared to healthy controls (mean value 5.9) but not indicative of a high level of sleepiness (135). It is however, equivalent to a commonly used cut-off for excessive daytime sleepiness (169). Daytime sleepiness was improved following treatment with BLT in our sample and, at the one-month follow-up, scores were equal to those in healthy controls (135, 146). In a study of treatment effects of BLT in persons with SAD and healthy controls (N=26) which had an open design, mood was improved and sleepiness reduced in patients with SAD following BLT (170), which corresponds to our results.

Level of fatigue was high in the sample at baseline (mean value for the FQ=19.3, SD=4.2) compared to the general population (mean value for the FQ=12.2, SD=3.9) (84). At the one-month follow-up, fatigue was improved and below the general population scores. To the best of our knowledge, measures of fatigue have not previously been used in clinical trials of BLT in SAD and S-SAD.

To summarize, in the merged group (N=47), fatigue, daytime sleepiness and health-related quality of life improved over time following bright light therapy (BLT) in a similar way to depressive mood.
Subgroups and treatment effects

Three distinct subgroups were identified in the sample in Study III, characterized by a common general high level of fatigue and differentiated from each other by varying levels of depression and sleepiness. Thus, one may argue that fatigue rather than depressive mood is the common, core symptom in SAD and S-SAD. On the basis of the similarities and differences, the three clusters were labelled Winter Fatigue and the three subgroups: Mildly depressed-Not sleepy, Mildly depressed-Sleepy and Depressed-Sleepy. Or in a more practical version: Simple winter fatigue, Winter fatigue with sleepiness and Winter depression. The clusters were validated on independent measures at baseline but not over time, since all subgroups improved following treatment with bright light.

There are a number of psychiatric studies using cluster analysis, but to the best of our knowledge, only one previous within the present domain. In that study, which was published in 1989, the cluster analysis was based on a measure of seasonality (the SPAQ) and results presented in the form of the subgroups “winter SAD and S-SAD” (171). The present subgroups analysis of a sample of persons with SAD and S-SAD, was based on measures of depression, fatigue and sleepiness. The results from our study support the common features in SAD and S-SAD rather than the differences and point to the importance of including a broader range of indicators of treatment effects in future clinical trials.

Methodological considerations

A major strength in Study I was the use of a random sample from the general population, stratified according to age, gender and home municipality. Even though the response rate was rather modest (66.3%), an interview with a relatively large random sample of the non-responders resulted in a fairly clear picture of the (low) prevalence figures among those not responding. In Study II, the sample was community-based, including all students of a certain age. The response rate was high (87.3%), which strengthens confidence in the results. Results from the prevalence studies should not be generalized to other areas in Sweden or elsewhere.

A major drawback for the SPAQ and the K-SPAQ is the lack of a specified time-window; there is no specification of which years the questions concern. The SPAQ and the K-SPAQ are both retrospective questionnaires with all the limitations inherent in such measures (172).

There is no agreement on how to define the seasons and, consequently, the definitions vary considerably between studies. Some authors use the definition of winter initially presented by Kasper et al (January and February) (17), which was based on the months in which there was the largest
proportion of persons responding “feeling the worst” in that particular area of the USA. Corresponding percentages for “feeling the worst” in the present study was 4.3% in September, 22% in October, 40% in November, 24% in December, 21% in January, 16% in February and 7.0% in March compared with for example 1% in June and July. Winter is a meteorological concept, defined according to the daily variations in temperature. Therefore the months included in the winter season vary not only between countries, but within a country like Sweden as well. Consequently it is reasonable that the definitions of the seasons differ between study areas. In the present study area, the meteorological beginning of autumn is in the middle of September. The winter starts in the middle of November and lasts until the end of March. Thus, in the present area of Sweden it seems reasonable to use a definition of the winter season as the period November through February and the autumn/winter season as the period October through February.

Is it possible, that the seasonal variations in mood and behavior described in this thesis and in a fairly large number of other studies, is merely a product of the use of one dominant measure, namely the SPAQ? To address this question, seasonal variation in depressed mood and emotions was measured prospectively for one year in healthy subjects (173). Results showed very clearly that there is a seasonal variation in emotions such as irritability, depressive mood and anxiety. The pattern was as expected, with lower levels of negative emotions during the summer and higher levels during the winter and the seasons, autumn and spring, in between these. The seasonal differences were more pronounced among women than among men.

In a recent review, the validity of the Hamilton Depression Rating Scale (HDRS) as a golden standard was questioned, mainly due to the multidimensionality of the scale and several single items that were considered to be of poor quality (143). A shorter version of the scale assessing depression severity along one dimension has been presented, but, unfortunately, this shorter version has not been adapted to fit the atypical symptoms found in SAD (174). Therefore, in spite of the limitations the SIGH-SAD/SR was judged to be the best available instrument when the present study was started.

**Internal and construct validity**

One major advantage in the clinical study was the randomisation of subjects, which is important in order to avoid selection bias in groups. Minimizing attrition is important for the same reason and attrition of subjects was considered to be rather low in the study. Two subjects were lost after randomisation, of which one was a dropout and the other excluded due to pregnancy. One limitation in the study was the lack of a systematic collection of data on side effects.

The aim of a waiting-list control group design (and no-treatment control group) is to control for possible threats to internal validity; i.e. extraneous factors that may account for the results, for example spontaneous remission
or the tendency of scores to regress towards the mean (statistical regression towards the mean). In a meta-analysis of outcomes from studies using a corresponding design in nonseasonal depression, the authors concluded that in the 4 to 8 weeks perspective, depressive symptoms can be expected to decrease 10-15% on average without treatment and as many as 20% of the subjects may experience a spontaneous remission (175). In the present study, the decrease of depressive symptoms in the control group was 2.3% during the three-week waiting period. Other threats to internal validity, such as the effects of repeated assessments, were not controlled for.

Construct validity concerns the issue of what specific aspects of the intervention were responsible for the change. Non-specific treatment effects were not controlled for in the study. It is most likely that a range of different factors affected the results, of which the light itself was only one. Examples of such factors are contacts with the staff and other patients, experimenter and staff expectations, having time for oneself in a relaxing atmosphere, getting up earlier than usual (phase advancing circadian rhythms) or factors in the physical environment. This does not necessarily imply that we could do without the light and still achieve similar good results. A non-specific treatment variable may or may not be effective on its own, but most probably influences the results in combination with the specific treatment variable; i.e. there is an interaction effect. What is suggested then, is to explore the different variables and how they interact with each other (176).

The importance of studying mechanisms of therapeutic change was discussed by Kazdin and Nock (177). Therapy refers to a broader view on interventions than just techniques. How can we help people to reduce negative symptoms, to find more adaptive functioning or more positive coping methods? If BLT is not just a matter of light, but light in combination with psychological, cognitive and behavioural factors, then the relation and relative importance between these variables can be investigated. Randomised, controlled clinical trials are the golden standard for evaluating the effects of treatments, but may be used for understanding the moderators and mediators of therapeutic change as well (178). Mediators are related to why and how an intervention can have an effect, while moderators are related to whom may benefit from the intervention and under what circumstances. A mediator is something that occurs during the treatment while a moderator precedes treatment. For example, the effect of BLT may partly be mediated through a reduction of catastrophic cognitions regarding the winter period and an increase in adaptive coping behaviours. But the effect may be limited to persons with a specific vulnerability.

**External validity**

External validity refers to the extent to which the results can be generalized to other samples and situations. It is for example related to the sample, to the intervention and to statistical validity. The sample in the clinical study had a
variation of symptoms ranging from mild to moderate/severe. The intervention was carried out in four already existing light rooms, with slightly different physical environments, light intensities and personnel. Treatment effects were assessed with multiple measures and results were clearly positive and synchronous. The treatment effects were similar in the subgroups. Even though the sample was rather small, the statistical power was adequate. These factors can be considered positive for the extent to which results can be generalized, because in clinical practice patients present with some variety of symptoms and light rooms and personnel vary as well. On the other hand, the persons participating in the study were not recruited from a patient population but from a general population sample, which limits the external validity. The results are therefore not necessarily representative for a patient population. Other aspects of external validity that cannot be ruled out in this study are the novelty effect, the mere awareness of participation in a study or pre-test sensitization. Results should be considered preliminary until replicated in other samples and with other types of designs, since replication is important for increasing the external validity of findings.

Clinical implications and future research

Life time prevalence of depression in the western world is approximately 17-18% and figures are rising, mainly due to an increase in mild and moderate depressions (8). Depression is a disorder with a high risk for relapse and is often chronic and life-long. In Sweden, the increase in numbers of sick-listed during the past ten years, were associated with a corresponding increase in depression (8). The personal and societal costs for depression are significant. There are some studies reporting that 10 to 11% of persons with depression have a seasonal depression (26, 27) which indicates that a substantial number of persons may suffer from SAD. There are also indications that a majority do not receive a correct diagnosis (33). There are some reports of patients with SAD being “heavy users” of primary health care; significantly more visits, prescriptions, investigations and referrals compared with matched controls with low seasonality scores (179). Even subclinical depression may be related to a substantial impairment (8). A study on the prevalence of seasonal depression in primary and psychiatric health care is therefore, a suggested future study.

As discussed previously, the Seasonal Pattern Assessment Questionnaire (SPAQ) is a measure of seasonality rather than of seasonal depression. Some years ago Thompson and co-workers developed the Seasonal Health Questionnaire (SHQ) to be used for prevalence studies in the general population (180). The SHQ is more closely related to the clinical diagnosis and a Swedish version of this questionnaire is currently being validated in patients with seasonal and nonseasonal depression.
The clinical use of BLT in patients with seasonal depression controlling for non-specific factors such as the attention provided by the staff, is indicated as another important future area of study. The effects of a combination of different treatments in SAD ought to be further investigated, for example combining psychotherapy with BLT and/or with medication. Other treatments, such as physical exercise, regular outdoor walks during daylight or physical exercise in a gym combined with bright light, warrant further investigation, especially for persons with winter fatigue and no depression (181, 182). If the subgroups identified in the study can be replicated in other samples, there is a further possibility to investigate other types of treatments, especially for the mildly depressed subgroups.

There are some studies indicating a relation between season, light, eating and mood. A recent controlled study showed that light therapy in combination with a moderate physical exercise program over a period of six weeks resulted in a slightly more effective weight reduction in overweight/obese women (183). Carbohydrates, especially sweet and simple ones like sucrose, affect the mood of depressed persons (184). In rats, photoperiod affected sucrose consumption and adiposity; during short but not long days, sugar consumption and adiposity increased (185). Other studies in healthy persons with seasonal symptoms indicate that the effect of exercise is more effective if combined with bright light (182, 186). Even though the relation between bright light and weight (reduction) is yet to be proven, it deserves further investigation.
Summary and conclusions

- Prevalence of winter depressive mood (“SAD” and “S-SAD”) was approximately 20% in adults and among adolescents after puberty. The results indicate that experiencing an increase in fatigue, lowered mood, sleep duration, appetite and weight are common during the winter season, even among people otherwise considering themselves healthy. The character of the seasonal symptoms was similar in the adult and adolescent samples.

- Treatment with bright light (in a light room) resulted in reductions of depressed mood in a sample of persons recruited from the general population, with clinically assessed Seasonal affective disorder (SAD) and Subclinical SAD (S-SAD). The positive results were maintained for at least one month.

- Treatment with bright light also reduced fatigue, daytime sleepiness and improved self-ratings of mental health (i.e. health-related quality of life). The positive results were maintained during the one-month follow-up.

- Three distinct subgroups were identified in the sample. A common factor in all three subgroups was a high level of fatigue compared to norms, hence the denomination Winter Fatigue. The following labels were used for the subgroups (1) Simple winter fatigue, (2) Winter fatigue with sleepiness and (3) Winter depression. Treatment was effective in all three subgroups.

Taken together, the results of this thesis suggest that winter fatigue and winter depression are common in the general population and that treatment with bright light can alleviate the symptoms and improve health-related quality of life. Results from the controlled clinical study confirm those of a previous published open study, which reported a positive effect from treatment with bright light in a light room, which is the type of bright light therapy generally provided in Swedish health care.
Sammanfattning på svenska


Av de fyra artiklar som ingår i avhandlingen är två epidemiologiska studier som undersöker förekomst av vinterrelaterade sytontom bland vuxna respektive ungdomar som går på gymnasiet. De övriga två artiklarna redovisar resultat från en behandlingsstudie med ljusterapi.

I det första delarbetet undersökt undersöktes förekomst av vinterrelaterade sytontom bland slupmässigt urval på 1657 personer mellan 18 och 65 år från fem kommuner i Dalarna (Avesta, Borlänge, Falun, Gagnef och Säter). Urvalet var proportionellt (stratifierat) med avseende på kön, ålder och hemkommun. Svarsfrekvensen uppgick till 66%. En analys av eventuella årstidsrelaterade sytontom bland dem som inte svarat på enkäten gjordes via en telefonintervju med 9% av bortfallet (dvs de som inte svarat på enkäten). Det andra delarbelet tog upp liknande frågor bland 756 ungdomar mellan 17 och 18 år, som gick andra året på någon av Falu Kommuns gymnasieskolor. Svarsfrekvensen var 87%.


Studien var en randomiserad, kontrollerad klinisk studie med väntelistedesign. Det gick till så att när försökspersonerna under hösten/vintern återigen kände av sina vinterrelaterade symtom, fick de fylla i en rad frågeformulär och först efter detta slumpades de antingen till experimentgruppen, som fick behandling direkt med tio dagars ljusterapi eller till kontrollgruppen, där behandlingen genomfördes efter tre veckors väntetid. Behandlingarna utfördes under 1,5 - 2 tim dagligen på morgonen under tio dagar under perioden oktober till och med februari i något av de fyra ljusrummen som ingick (Sömnlab på Avesta Lasarett, Psykiatriska öppenvårdsmottagningen i Falun, Gagnefs vårdcentral eller akutmottagningen vid Säters sjukhus). Uppföljande mätningar gjordes en månad efter avslutad behandling. De frågeformulär som användes var SIGH-SAD/SR (en version av Hamilton Depression Scale som är ett självskattningsformulär för depressiva symtom), Fatigue Questionnaire (en självskattning av brist på energi eller känsla av matthet), Epworth Sleepiness Scale (självskattning av sömnhet, tendens att somna på dagtid i olika situationer) och SF-36 som mäter hälsorelaterad livskvalité (självskattad mental och fysisk hälsa). Deltagarna fick också fylla i några frågor om förväntningar på behandlingen.

Resultaten från den kliniska studien var positiva. Depressionsgraden minskade ≥50% hos 13 av de 24 i behandlingsgruppen, medan ingen i kontrollgruppen fick en motsvarande förbättring. Vid uppföljning en månad senare var 39 av de 47 i den sammanslagna gruppen ≥50% förbättrade. Fatigue (brist på energi), sömnhet, och självskattad mental hälsa (i frågefor-
muläret om hälsorelaterad livskvalitet), som var sämre än genomsnittligt/normalt före behandlingen, förbättrades på ett liknande sätt som grad av depression. Effekterna kvarstod vid uppföljningen efter en månad. Studien undersökte effekterna av ljusterapibehandlingen som helhet, men för att få kunskap om vilka delar av behandlingen som är centrala för att den positiva effekten ska erhållas, behövs kliniska studier med annan uppläggning (design).

I det fjärde delarbetet undersöktes förekomst av subgrupper bland dem som deltagit i den kliniska studien. Utifrån personliga svarsmönster på de frågeformulär som mätte depressionsgrad, fatigue (brist på energi) och sömnighet, identifierades tre undergrupper. Alla tre grupperna hade det gemensamt att de hade en högre nivå än genomsnittligt för befolkningen på grad av fatigue (brist på energi), medan det fanns olika (låg respektive hög) nivå av depressiva symtom och sömnighet i grupperna. En gemensam benämning för de tre grupperna blev därför ”Vintertrötthet och Vinterdepression”, medan de enskilda subgrupperna fick benämningarna ”Okomplicerad vintertrötthet”, ”Vintertrötthet med sömnighet” och ”Vinterdepression”. Alla de tre undergrupperna förbättrades av behandling med ljusterapi.

Resultaten sammantaget tyder på att vintertrötthet och vinterdepression är vanligt förekommande i befolkningen och att behandling med ljusterapi kan lindra symtomen och förbättra livskvaliteten, speciellt med avseende på den mentala hälsan. Resultaten från den kontrollerade kliniska studien bekräftar tidigare publicerade resultat från en studie med ljusbehandling i ett ljusrum, som är den typ av ljusterapi som vanligtvis används i svensk sjukvård.
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A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)