From
The OLIN Study Group and Division of Respiratory Medicine and Allergy,
Department of Medicine, Sunderby Central Hospital of Norrbotten.
Department of Respiratory Medicine and Allergy, University of Umeå.
Respiratory Unit, National Institute for Working Life, Stockholm, Sweden.

SNORING AND OTHER SYMPTOMS RELATED TO OBSTRUCTIVE SLEEP APNEA

Prevalence, Risk Factors, And Relation To Respiratory Disorders

The Obstructive Lung Disease in Northern Sweden Study III

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Av

Lars-Gunnar Larsson

Fakultetsopponent: Professor Per Bakke
Lungavdelningen, Haukelands Sjukhus, Bergen, Norge
Abstract: SNORING AND OTHER SYMPTOMS RELATED TO OBSTRUCTIVE SLEEP APNEA; prevalence, risk factors, and relation to respiratory disorders - The Obstructive Lung Disease in Northern Sweden Study III - Lars-Gunnar Larsson

These studies are a part of the Obstructive Lung Disease in Northern Sweden Studies (OLIN), an epidemiological research program in Northern Sweden. The aim of this thesis was to examine the prevalence of symptoms related to Obstructive Sleep Apnea Syndrome (OSAS) in Norrbotten, their relation to lung function, respiratory diseases including bronchitis, asthma and rhinitis, to examine risk factors, gender differences, and to the extent to which subjects with symptoms related to OSAS have received attention in the public health care system. A further aim was to validate whether snoring as a problem predicts obstructive sleep apnea (OSA).

In 1991 a questionnaire was sent by mail to a bronchitic cohort where 450 of 523 (86%) participated, and to a respiratory healthy control group where 529 of 625 (85%) participated in three age groups, 41-42 y, 56-57 y, and 71-72 y. The survey was followed by lung function tests and clinical examinations (n=579). Overnight sleep recordings were done in subjects reporting snoring as a problem (n=52). A second survey by mail was performed in 1992 in a representative sample of men and women aged 20-69 y, and 4648 of 5424 (86%) subjects responded. The OLIN questionnaire about respiratory symptoms and diseases, smoking habits, and profession with additional questions about sleep disturbances was used in the two surveys. The studies were performed in Norrbotten, which is the northernmost province of Sweden.

In the bronchitic cohort the prevalence of symptoms related to OSAS was higher than in the control group, snoring as a problem 23 vs. 12%, witnessed apneas 18 vs. 8.3%, nod off 16 vs. 7.0%, and not rested after a full nights sleep, 33 vs. 28% respectively. Subjects with recurrent wheeze, chronic productive cough, or sputum production reported snoring as a problem and witnessed apneas twice as often as subjects in the healthy cohort. Bronchitic symptoms but not lung function impairment was associated with snoring as a problem or witnessed apneas. The sleep studies showed that subjects with bronchitis were found to have obstructive sleep apnea twice as often as subjects without respiratory symptoms. The minimum prevalence for OSA (AHI ≥ 10) with concomitant daytime sleepiness (OSAS) was 5.4% in subjects with bronchitic symptoms and 2.3% in the respiratory healthy.

In the population study 11% (15 in men, 6.7% in women) reported snoring as a problem. The prevalence increased with age with a peak prevalence in men at 55-59 y (28%), and in women at 60-64 y (14%), while declined in the elderly. Relatives’ concerned about witnessed sleep apneas was reported by 6.8% (11% in men, 2.4% in women). The age distribution of witnessed apneas was the same as in snoring with peaks in the same age groups, 21% in men aged 55-59 y, and 6.5% in women aged 60-64 y. Daytime sleepiness was more common in subjects reporting snoring as a problem, especially in women, in whom not rested after a full night sleep was reported by 50% vs. 40% among men. Snoring as a problem was more common in subjects with concomitant respiratory symptoms: among subjects with chronic bronchitis 26%, physician-diagnosed asthma 20%, and rhinitis 15% vs. 10% in subjects without these disorders. Age, male gender, current smoking, chronic bronchitis, asthma, and rhinitis were independently associated with snoring as a problem, as analysed by multiple logistic regression.

Between 1990 and 2000, 3955 subjects (2991 men, 964 women) aged 20-69 were referred to the Department of Respiratory Medicine in Boden/Sunderby Hospital for sleep studies due to symptoms related to OSAS. The estimated prevalence of snoring as a problem or witnessed apneas in our study was 17.9% in men, and 7.4% in women. By presuming that the prevalence has been stable, we can estimate that during a 10-year period approximately 20% of men and 16% of women with these symptoms have been referred for sleep studies. According to prevalence of symptoms in our study, women with snoring as a problem or witnessed sleep apneas were less likely to have been referred for a sleep study than men, although they had reported more daytime sleepiness symptoms.
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This thesis is based on the following papers:


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To Anne
Lasse and Karin
Linnea
Felix
# CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>1</td>
</tr>
<tr>
<td>LIST OF ORIGINAL PAPERS</td>
<td>2</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>4</td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td>6</td>
</tr>
<tr>
<td>TERMS AND DEFINITIONS</td>
<td>7</td>
</tr>
<tr>
<td>BACKGROUND</td>
<td>9</td>
</tr>
<tr>
<td>PERSONAL REFLECTIONS</td>
<td>9</td>
</tr>
<tr>
<td>HISTORICAL FLASHBACK</td>
<td>10</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>12</td>
</tr>
<tr>
<td>PATHOGENESIS</td>
<td>12</td>
</tr>
<tr>
<td>SIGNS AND SYMPTOMS</td>
<td>14</td>
</tr>
<tr>
<td>DIAGNOSTIC PROCEDURES</td>
<td>18</td>
</tr>
<tr>
<td>EPIDEMIOLOGY</td>
<td>19</td>
</tr>
<tr>
<td>Prevalence</td>
<td>19</td>
</tr>
<tr>
<td>Risk factors</td>
<td>21</td>
</tr>
<tr>
<td>CONSEQUENCES</td>
<td>25</td>
</tr>
<tr>
<td>TREATMENT</td>
<td>27</td>
</tr>
<tr>
<td>AIMS</td>
<td>32</td>
</tr>
<tr>
<td>METHODS</td>
<td>33</td>
</tr>
<tr>
<td>STUDY AREA</td>
<td>33</td>
</tr>
<tr>
<td>STUDY DESIGN</td>
<td>33</td>
</tr>
<tr>
<td>STUDY POPULATION</td>
<td>33</td>
</tr>
<tr>
<td>POSTAL QUESTIONNAIRE</td>
<td>37</td>
</tr>
<tr>
<td>CLINICAL INVESTIGATIONS</td>
<td>37</td>
</tr>
<tr>
<td>DETERMINANTS OF DISEASE AND DIAGNOSTIC CRITERIA</td>
<td>38</td>
</tr>
<tr>
<td>SLEEP STUDIES</td>
<td>39</td>
</tr>
<tr>
<td>ANALYSES AND STATISTICAL METHODS</td>
<td>39</td>
</tr>
<tr>
<td>ETHICAL ASPECTS</td>
<td>40</td>
</tr>
</tbody>
</table>
ABBREVIATIONS

AI Apnea Index
AHI Apnea Hypopnea Index
BMI Body Mass Index, (body weight divided by the square of body height, kg/m²)
CB Chronic Bronchitis
COPD Chronic Obstructive Pulmonary Disease
CPAP Continuous Positive Airway Pressure
EDS Excessive Daytime Sleepiness
EEG Electroencephalography
EMG Electromyography
ESS Epworth Sleepiness Scale
FEV₁ Forced Expiratory Volume in one second
FVC Forced Vital Capacity
MSLT Multiple Sleep Latency Test
nCPAP nasal CPAP
OSA Obstructive Sleep Apnea
OSAS Obstructive Sleep Apnea Syndrome
PSG Polysomnography
QoL Quality of Life
REM Rapid Eye Movement
SDB Sleep Disordered Breathing
UARS Upper Airway Resistance Syndrome
UPPP Uvulopalatopharyngoplasty
TERMS AND DEFINITIONS

APNEA

Cessation of airflow for at least 10 s (Guilleminault et al, 1976).

Central apnea
Apnea without inspiratory effort.

Obstructive apnea
Apnea with inspiratory effort.

Mixed apnea
Apnea starts as a central apnea and is followed by an obstructive component with inspiratory effort during the last part of the apnea (Gaustaut, 1965).

HYPOPNEA

Most authors define hypopnea as a reduction in airflow to at least 50%, and lasting for a minimum of 10 s. Some authors require concomitant oxygen desaturation or arousal (Gould et al, 1988; American Sleep Disorders Association, 1990; Moser et al, 1994; Redline & Sanders, 1997; Tsai et al, 1999). A hypopnea is classified as either central or obstructive (see apnea).

APNEA INDEX (AI)

Mean number of apneas per hour of sleep.

APNEA-HYPOPNEA INDEX (AHI)

Mean number of apneas and hypopneas per hour of sleep.
OBSTRUCTIVE SLEEP APNEA (OSA)

Early definition, an apnea index over 5 or at least 30 apneas during seven hour of nocturnal sleep (Guilleminault et al, 1976). Today different cut off levels such as an AI or AHI of 5, 10, 15 or 20 events/hour are discussed.

OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS)

OSA with concomitant daytime symptoms, such as excessive daytime sleepiness (EDS).

UPPER AIRWAY RESISTANCE SYNDROME (UARS)

Symptoms of increased upper airway resistance with snoring, excessive daytime sleepiness, and arousals, but without increased number of significant apneas or hypopneas (Guilleminault et al, 1993). Respiratory effort related arousal (RERA), is another term which describes polysomnographic findings in patients with UARS.

OVERLAP SYNDROME

Patients suffering from both obstructive sleep apnea and chronic obstructive pulmonary disease (COPD) (Flenley, 1985).
PERSONAL REFLECTIONS

When I was very young, I sometimes heard my father snore. My room was adjacent to my parent’s bedroom. I have forgotten if his snoring disturbed me then, but I don’t think he snored more than occasionally. After leaving home, I cannot remember that I ever thought about snoring. During my medical studies early in the 1970’s, snoring was not discussed at all. Eventually I specialised in pulmonary medicine in Boden, and during the 1980’s I read some papers about snoring and sleep apnea. A few years later I met the first patient with the diagnosis of Obstructive Sleep Apnea. He was investigated with polysomnography at the Department of Respiratory Medicine in Umeå, and was prescribed continuous positive airway pressure (CPAP) by mask. At that time it was a remarkable, noisy and heavy machine. In 1990, we introduced in-home overnight sleep recordings in Boden. Since then we have studied more than 3000 patients. Among these 3000 with snoring and suspected obstructive sleep apnea, I can still remember the first patient with a dramatic overlap syndrome. It was a 50 year old man with advanced COPD and a severe obstructive sleep apnea syndrome. He suffered from cor pulmonale, extreme hypersomnolence and severe cognitive dysfunction. After a few weeks on CPAP there was a remarkable change. He became alert and happy, the edema vanished and he said; “The world around me has regained its colors”. This dramatic therapeutic effect of CPAP in such a serious condition made a great impression on me, and the clinical picture with the combination of obstructive sleep apnea and chronic obstructive pulmonary disease caught my interest. Eventually the interest grew beyond what was already written, and this is how the work of this thesis began.
In classic literature there are several good descriptions of persons with typical sleep disordered breathing. According to Kryger (1983) Dionysius of Heracleia (c. 330 BC) was described by Aelianus, as a glutton who "increased to an extraordinary degree of corpulence and fatness" that he "had much ado to take breath". His physicians were instructed to continually wake him from sleep with long fine needles thrust into his flesh.

Perhaps the most famous historical presentation of sleep disordered breathing is Charles Dickens (1837) description in "The Posthumous Papers of the Pickwick Club" of Joe, the fat boy who snored heavily and fell asleep during the daytime. Joe "divided his time into small alternate allotments of eating and sleeping". The description of Joe is typical for a person with severe obstructive sleep apnea syndrome. Heavy snoring, daytime somnolence, cognitive impairment, and ultimately cor pulmonale. The term Pickwickian was introduced in the medical literature by Osler (1919) to describe patients with the combination of cor pulmonale, intellectual impairment and severe daytime somnolence. The term Pickwickian syndrome is still in use today to describe patients with extreme obesity and daytime hypersomnolence, clinical findings of respiratory failure and cor pulmonale due to hypoventilation.

In late 19th century, there were some observations that subjects with nasal obstruction had cognitive and intellectual dysfunction, reversed by treatment improving their nasal airflow (Hill, 1889; Wells, 1898). A typical obstructive sleep apneic event was described by Broadbent (1877); "there will be perfect silence through two, three, or four respiratory periods, in which there are ineffectual chest movements; finally air enters with a loud snort, after which there are several compensatory deep inspirations".

Technical advances in diagnostic procedures have made it possible to recognise sleep disordered breathing (SDB). The first step was the discovery of differences in electrical brain activity during sleep and wakefulness, the development of electroencephalography (EEG) 1928 (Berger, 1930). Sleep stages were identified, and in 1968 a generally accepted classification for sleep EEG came into use (Rechtschaffen & Kales, 1968). Measuring electric brain activity, rapid changes in arterial oxygen saturation, respiratory effort and oro-nasal air-flow has been crucial for understanding the obstructive sleep apnea syndrome. The first descriptions of polysomnographic findings
in patients with OSAS were published in 1965 (Gaustaut et al, 1965; Jung & Kuhlo, 1965).

Different treatment techniques have been introduced. Tracheostomy was reported by Kuhlo et al (1969) and Lugaresi et al (1970), then uvulopalatopharyngoplasty (UPPP) by Fujita et al (1981), and treatment with continuous positive airway pressure (CPAP) by Sullivan et al (1981). It was with the introduction of CPAP in 1981 that effective and non-invasive treatment for the masses of sleep-apneics became available.

Research in sleep disordered breathing has increased dramatically the last two decades. While our knowledge and understanding of sleep apnea has increased, there is still much to learn about pathogenesis, presentations, risk factors and consequences.
INTRODUCTION

PATHOGENESIS

Sleep disordered breathing (SDB) is an old reality but a new scientific entity. During the last decades it has been recognised and defined as partial or complete upper airway collapse, snoring with or without hypopneas or apneas. The disease has different degrees of severity from simple snoring, upper airway resistance syndrome (UARS) (Guilleminault et al, 1993; Shaheen et al, 1993; Gottlieb et al, 2000), to obstructive sleep apnea syndrome (OSAS) with daytime symptoms as hypersomnolence and excessive daytime sleepiness in addition to hypopneas and apneas (American Sleep Disorders Association, 1990; Stradling et al, 1991; Cheshire et al, 1992; Dealberto et al, 1994; Berry & Gleeson, 1997; Chervin, 2000). The disease is probably progressive, starting with simple snoring and developing into first mild and then severe OSAS (Svanborg & Larsson, 1993; Pendlebury et al, 1997; Lindberg et al, 1999).

APNEA

A typical obstructive sleep apneic event consists of an occlusion of the upper airway, most often at the level of the soft palate or at the base of the tongue. The arterial oxygen saturation decreases. During the breathing pause, the subject makes increasing inspiratory efforts, struggling for air. After a variable time, which can last from 10 seconds up to minutes, the apnea is interrupted by an arousal that ceases the obstruction of the upper airway, and breathing starts again.

COLLAPSE OF THE UPPER AIRWAYS

Complete or partial collapse of the upper airway during inspiration is the main event that results in apnea or hypopnea. During inspiration, a negative or suction pressure is created in the upper airway, and activity in the pharyngeal dilator muscles is necessary to keep the upper airways open during inspiration in the normal breathing cycle.
THE UPPER AIRWAYS

The upper airway is patent only if the dilator forces in the pharynx exceed the negative suction pressure during the inspiration. Pharyngeal anatomy, morphology and neuromuscular activity are involved during inspiration. Narrowing of the upper airway, for example, generates increased negative pressure during inspiration, and thereby enhances the risk for occlusion of the upper airways (Horner et al, 1991). Upper airway narrowing can be due to genetic or acquired morphological changes (Mathur & Douglas, 1995; Redline et al, 1997a), intra pharyngeal fat or fat localised around the neck (Davies et al, 1993; Shelton et al, 1993a; Shelton et al, 1993b; Mortimore et al, 1998; Sakakibara et al, 1999). Nasal obstruction (Young et al, 1997c), diseases such as myxedema and acromegaly (Orr et al, 1981; Grunstein et al, 1994a) or adenotonsilar hypertrophy (Mangat et al, 1977; Stradling et al, 1990) are other predisposing factors to obstructive sleep apnea.

MUSCLE ACTIVITY AND VENTILATORY CONTROL

The pharyngeal dilator muscle activity is essential to keep the upper airway open. These different muscle groups are activated in co-ordination before the diaphragm contracts, and hypoxia, hypercapnia and negative intraluminal pharyngeal pressure are factors that augment the drive of upper airway dilator muscles. In patients with OSA it has been shown that the muscle activity is reduced and discoordinated during sleep (Remmers et al, 1978; Kimura et al, 1994). Two possible mechanisms have been proposed for this phenomenon. Influence from sleep fragmentation with an increased demand on activity from this muscles will lead to muscular lesions related to overwork causing muscular fatigue and biochemical changes (Fleury, 2000). The other possible mechanism is repeated mechanical muscle trauma from vibration of the soft palate during snoring, damaging neuromuscular function (Woodson et al, 1991; Larsson et al, 1992; Series et al, 1996; Friberg et al, 1998). Further, deteriorated ventilatory control associated with blunting of the hypoxic ventilatory response may contribute to obstruction of the upper airways by reduced dilator muscular response to inspiration (Redline et al, 1997a).
AROUSAL

An arousal is a short awakening with associated EEG alpha rhythm, and lasting for 3-15s. Arousals are often seen with an increase in electromyogram (EMG) tone (American Electroencephalographic Society, 1994). Arousal from sleep is a protective mechanism to keep the upper airway patent. Hypercapnia is a potent stimulus for arousal (Hedemark & Kronenberg, 1982; Berthon-Jones & Sullivan, 1984; Verbraecken et al, 1995). An apnea is generally terminated by an arousal (Remmers et al, 1978; Issa & Sullivan, 1984), and is usually followed by a period of hyperventilation. Repeated arousals lead to sleep fragmentation, which also predisposes to worsening of the sleep apnea pattern (Guilleminault & Rosekind, 1981).

SIGNS AND SYMPTOMS

Snoring, apneas and excessive daytime somnolence (EDS) are the main findings in OSA.

SNORING

Snoring is a sound that is generated by vibrations from partially collapsed upper airways. The noise can disrupt the snorer’s sleep, as well as the sleep of a bed partner. The average level of snoring sound intensity is reported to be higher in men than in women, and is associated with body mass index, and also with AHI (Wilson et al, 1999). Snoring is almost always present in OSA, except in some cases of UARS as well as after uvulopalatopharyngoplasty (UPPP) where snoring can be abolished despite persistent apneas (Guilleminault et al, 1993; Davis et al, 1993). The reduction of tissue in the soft palate after UPPP makes the sound generating vibrations less intense, and obstructive apneas can occur without loud snoring. Snoring is often worse in supine position (Lugaresi et al, 1988; Bahammam et al, 1999), as well as with reduced muscular tone after sleep deprivation or after intake of alcohol or sedatives (Lugaresi et al, 1988).
APNEAS

An apnea in adults is defined as cessation of airflow for at least 10s (Guilleminault et al, 1976).
Apneas are defined as central, obstructive or mixed.
A central apnea is cessation of airflow due to lack of neural output from the respiratory centre in the brainstem and thus without inspiratory effort.
An obstructive apnea is due to upper airway obstruction and is associated with inspiratory effort, the subject is struggling for air.
Mixed apnea is an apnea that starts as central, and is followed by an obstructive component with inspiratory effort during the last part of the apnea (Gaustaut et al, 1965).
Sometimes the snorer wakes up with a feeling of choking and panic after an apnea (Edlund et al, 1991), and bed-partners often report that they are anxious about breathing pauses of their snoring partner which make them stay awake.

DAYTIME SLEEPINESS AND SOMNOLENCE

Daytime sleepiness or daytime hypersomnolence is the most common symptom of OSA (Wetter et al, 1994; Redline et al, 1997b; Lindberg, 1998). It is mainly due to arousal-induced sleep fragmentation (Roehrs et al, 1989; Sforza & Krieger, 1992; Martin et al, 1997; Bennett et al, 1998), but hypoxia may contribute (Punjabi et al, 1999). Repeated arousals throughout the night lead to deteriorated sleep quality. The normal sleeping pattern is disrupted in subjects with sleep apnea leading to physical and psychological negative consequences. Daytime hypersomnolence is often referred to a feeling of not being refreshed after a whole night's sleep or having a tendency to fall asleep during breaks in activity in the daytime. Questionnaires such as the Epworth Sleepiness Scale (ESS), are the most common approach to estimate daytime sleepiness (Johns, 1993). ESS consists of questions about estimated risk for dozing off in various situations. A more objective way to estimate EDS is by instrumental tests. Multiple sleep latency test (MSLT) (Carskadon et al, 1986; Carskadon, 1993) is the generally accepted reference method among such tests. It measures, using EEG criteria, the mean time to fall asleep under standardised conditions. The association between ESS and MSLT is significant but not strong, and they probably measure different aspects of somnolence (Olson et al, 1998). Other tests measure vigilance in specified situations, for example car-driving (George et al, 1996; George et al, 1997)
or how disorders of excessive sleepiness affect patients abilities to conduct normal activities (Weaver et al, 1997). Although these tests measure different aspects of somnolence, they all show a positive association with sleepiness and OSA (Carskadon, 1993; Johns, 1994; George et al, 1996; George et al, 1997). Ulfberg et al (1996a) reported that the risk ratio for EDS at work was 4-fold for snorers in a general population, 20-fold for snoring patients, and 40-fold for patients with OSAS compared with non-snoring men in the general population. In the same study, patients with snoring or OSAS had difficulties with concentration, learning new tasks, and performing monotonous tasks.

COGNITIVE DYSFUNCTION

Cognitive function contains many different aspects, which can be affected by obstructive sleep apnea. Memory function, ability to pay attention, concentrate, and to solve complex problems are of great importance for social, emotional and professional life. Some of these cognitive functions, which require sustained attention, are sensitive to sleepiness, whereas disturbances in memory and motor skill are thought to be more related with hypoxia. It is thus expected that cognitive functions closely related to sleepiness are impaired in patients with OSA (Jennum & Sjol, 1994; Roehrs et al, 1995). Redline et al (1997b) reported vigilance deficit in patients with mild OSA though they did not find any substantial sleepiness or appreciable deficits in more complex neuropsychological processes. Others have reported associations between OSA and cognitive dysfunction in different aspects (Kales et al, 1985; Cheshire et al, 1992; Naegle et al, 1995). Continuous positive airway pressure (CPAP) therapy seems to reverse most of the symptoms, except short-term memory dysfunction (Naegle et al, 1998; Loube & Andrada, 1999; Munoz et al, 2000).

DEPRESSION AND ANXIETY

There are several reports where subjects with OSA had a high rate of depressive mood disorders (Balan et al, 1998; Bardwell et al, 2000; Yamamoto et al, 2000), but others have found neither significant association between depression and snoring nor positive effect on mood in patients with OSA after starting CPAP-treatment (Engleman et al, 1993; Pillar & Lavie, 1998; Munoz et al, 2000). It is possible that fatigue, tiredness and lack of
energy that are common in subjects with OSA is confounders in evaluating mood disorders (Chervin, 2000).

MORNING HEADACHE

Morning headache is common in subjects with snoring or OSA (Jenum & Sjol, 1993; Jennum & Sjol, 1994; Ulfberg et al, 1996b; Harding, 2000), and treatment with CPAP or UPPP can reduce these headaches (Loh et al, 1999). SDB has also been found in a majority of patients with cluster headache (Chervin et al, 2000).

QUALITY OF LIFE

Quality of Life (QoL) is strongly affected by OSA. Both self-assessed quality of life questionnaires and standardised tests such as Short Form-36 Health Survey Questionnaire (SF-36), Functional Limitations Profile (FLP), the EuroQol (EQ-5D) and Munich life-quality dimension list (MLDL), have found reduced QoL in subjects with OSA (Grunstein et al, 1995b; Jenkinson et al, 1997; Yang et al, 2000). Effective treatment with CPAP reverses the impairment in quality of life (Bolitschek et al, 1998; Kingshott et al, 2000).

POLYURIA

Nocturnal polyuria is a very striking and common symptom in OSA. One of the most astonishing findings that patients experience when they start therapy with CPAP is the instant abolishment of polyuria the first night on effective treatment. Atrial natriuretic peptide is elevated during sleep in patients with OSA. This is probably due to hemodynamic changes during sleep in obstructive apneas, and this increased secretion of atrial natriuretic peptide is responsible for high salt elimination and hence the increased urine production seen in OSA (Krieger et al, 1988; Warley & Stradling, 1988; Baruzzi et al, 1991). The plasma levels of atrial natriuretic peptide have been shown to be associated with the degree of hypoxia and the degree of esophageal pressure swings during the sleep apneas. Atrial natriuretic peptide is released in response to atrial stretch. Hypoxia may act by increasing the pulmonary artery pressure due to hypoxic vasoconstriction, and the repeatedly increased intra-thoracic pressures may act as a pump.
sucking blood into the thorax and increase the cardiac afterload (Krieger et al, 1991).

OTHER SYMPTOMS

Other common complaints among patients with OSA are arousals with a choking feeling and sometimes profuse body sweating during sleep (Whyte et al, 1989; Ambrogetti et al, 1991). Erectile dysfunction is common (Hirshkowitz et al, 1990), and this seems to be related to autonomic nervous system dysfunction. The development of autonomic dysfunction is associated with nocturnal hypoxia and a more severe degree of OSAS (Fanfulla et al, 2000). Treatment with CPAP relieved erectile dysfunction in one-third of patients (Karacan & Karatas, 1995).

DIAGNOSTIC PROCEDURES

OSA

An apnea in adults is defined as cessation of airflow for over 10 s. In obstructive sleep apnea it is accompanied by inspiratory efforts (Guilleminault et al, 1976). In 1988 the term hypopnea was introduced, describing events with the same physiological consequences as apneas, but with a reduction instead of cessation of airflow (Gould et al, 1988). It is most often referred to a 50% reduction in airflow (Moser et al, 1994) with concomitant arousal or oxygen desaturation according to American Sleep Disorders Association (American Sleep Disorders Association, 1990).

Apnea index (AI) or Apnea-Hypopnea Index (AHI) is used to quantify sleep disturbances. They refer to the average number of apneas or average number of apneas and hypopneas per hour of sleep. Clinical significant OSA was first defined as AHI > 5 (Guilleminault & Dement, 1978). The way to diagnose obstructive sleep apnea is to perform over-night sleep studies. Much interest has been focused on questionnaires and combinations of questionnaires, clinical findings and oxymetry in order to limit the number of patients referred to sleep lab for polysomnography (PSG) (Crocker et al, 1990; Viner et al, 1991; Haraldsson et al, 1992; Kump et al, 1994; Deegan
Though many different initial assessments are somewhat predictive of OSA, no diagnostic routine has yet succeeded to give enough predictive value to make sleep studies unnecessary.

POLYSOMNOGRAPHY

The generally accepted reference method for sleep apnea recordings is polysomnography. PSG is recommended by the American Sleep Disorders Association, for the diagnosis of sleep-related breathing disorders, for continuous positive airway pressure (CPAP) titration and for the assessment of treatment results (American Sleep Disorders Association, 1997). Polysomnography most often includes EEG, electro-oculogram, chin-electromyogram, nasal and oral airflow, abdominal and chest movement detection, pulse oxymetry, body position, electrocardiogram and leg movement detection (American Electroencephalographic Society, 1994).

PORTABLE IN HOME RECORDINGS

Technologic advances have made it possible to develop portable recording devices for sleep studies. These devices have simplified sleep apnea recordings and they provide a comfortable and reliable way of in-home monitoring of a sufficient number of parameters for the diagnosis of OSA. They have made it possible to perform sleep studies in a greater scale according to actual demand in the population. If the diagnosis remain unclear, further investigations with PSG should be performed (Stoohs & Guilleminault, 1992; American Sleep Disorders Association, 1994; Orr et al, 1994; Zucconi et al, 1996; Parra et al, 1997).

EPIDEMIOLOGY

PREVALENCE

Obstructive sleep apnea is common in the general adult population. Prevalence rates are dependent on the definition and the studied population,
as age, gender, estimation of daytime sleepiness, and cut off point for AHI strongly affects the prevalence rates.

Snoring

Prevalence rates for snoring vary considerably. Differences in the definition of habitual snoring, the age composition of the population under study, and the method used have contributed to variations in reported prevalence. Habitual snoring is generally defined as snoring every, or almost every night. In some studies it is defined as snoring every, or a specified number of nights a week, and in some reports defined as always, or often snoring. Habitual snoring is reported in 9%-48% in men and in 4%-34% in women. Habitual snoring is about twice as prevalent in men as in women (Gislason et al, 1988; Young et al, 1993; Ferini-Strambi et al, 1994; Stradling & Crosby, 1991; Ohayon et al, 1997; Neven et al, 1998; Jennum & Sjol, 1992; Enright et al, 1996; Lindberg et al, 1998c; Bixler et al, 1998).

Apneas

Witnessed sleep apneas are less common than snoring. Apnea has been reported in 4.4%-5.4% of men and in 2.1%-2.4% of women (Ohayon et al, 1997; Marin et al, 1997). In Tucson, Enright et al (1996) found high prevalence for self reported apneas in elderly (65 years and older), with 13% of men and 4% of women reporting that relatives had observed apneas. Apneas during sleep are either obstructive or central. Central apneas are related with heart failure (Tremel et al, 1999; Franklin et al, 1997), and some studies indicate that it is especially central apnea that increases in frequency in the oldest age groups (Bixler et al, 1998).

Osas

Most population based epidemiological studies have started with a screening procedure in order to find subjects at risk for obstructive sleep apnea. Sleep studies have then been performed in this high-risk sample to verify the diagnosis. These studies therefore express the lower limit of prevalence for OSAS. Significant OSAS is reported in 0.3%-3.3% in men (Cirignotta et al, 1989; Bixler et al, 1998; Neven et al, 1998; Hui et al, 1999) and in 0.9%-

20
2.5% in women (Jennum & Sjol, 1992; Gislason et al, 1993). In the hitherto largest study consisting of a random sample of state employees aged 30-60 years in Wisconsin USA, Young et al (1993) found a prevalence for AHI≥10 of 15% in men and 5% in women. Corresponding figures for AHI≥10 with concomitant excessive daytime sleepiness was 2.3% in men and 1.1% in women.

RISK-FACTORS

Gender

Male gender is a risk factor for snoring and sleep apnea. Men are affected twice as often as women in epidemiological studies. In sleep clinics the men/women ratio is considerably higher, 8 - 10 to 1 (Guilleminault et al, 1988a; Young, 1993; Redline et al, 1994; Young et al, 1997b). The gender differences may partly be explained by differences in body fat distribution (Young, 1993), and in different upper airway anatomy or pharyngeal dilator muscle function (Popovic & White, 1998; Pillar et al, 2000). Snoring in women increases after menopause. Progesterone and estrogen has been proposed to exert a protecting effect during the fertile period (Guilleminault et al, 1988a). Short-term hormone replacement therapy with either estrogen alone or in combination with progesterone has given divergent results. Some studies have shown a reduction in clinical severity of obstructive sleep apnea in postmenopausal women (Pickett et al, 1989; Keefe et al, 1999), while in other studies no beneficial effect of hormone therapy could be seen. (Franklin et al, 1991; Cistulli et al, 1994).

Age

Most studies have found self-reported snoring and apneas in adults to increase with age, with a peak at 55-60 years of age. In the elderly, a decrease in snoring prevalence is commonly found (Gislason et al, 1988; Ohayon et al, 1997; Bixler et al, 1998). This age-related difference in prevalence of snoring is probably correct and not due to age-differences in reporting (Lindberg et al, 2000). Also, prevalence of OSAS increases with
Obesity

Snoring and OSA are strongly associated with obesity. About 70% of patients with OSAS are obese (Bloom et al, 1988; Vgontzas et al, 1994). A 10% increase in weight predicted a 6-fold increase in the odds of developing moderate to severe SDB (Peppard et al, 2000a). Some authors report a narrowing effect of the upper airways due to deposition of fat in the pharynx (Shelton et al, 1993a), but fat deposition around the neck may also contribute (Davies & Stradling, 1990; Hoffstein & Mateika, 1992). Others have found a better association between OSA and central obesity and claim that waist circumference is a better predictor of sleep apnea than neck circumference or BMI (Grunstein et al, 1993).

Smoking

Current smoking is a risk factor for snoring in both sexes (Bloom et al, 1988; Delasnerie-Laupretre et al, 1993; Lindberg et al, 1998c; Hu et al, 1999). Whether smoking is an independent risk factor or if it acts through bronchitis is not clarified. The mechanism is unclear. Inflammatory changes in the upper airway may contribute to morphological changes of the upper airway. Some authors suggest that the association between smoking and snoring might be due to a direct nicotine effect (Wetter et al, 1994).

Rhinitis

Nasal obstruction can in predisposed individuals contribute to snoring, sleep fragmentation and OSA. Nasal breathing seems to be the preferred normal route during sleep, and nasal obstruction will frequently lead to nocturnal mouth breathing and snoring (Scharf & Cohen, 1998). Nasal obstruction is perhaps more likely to cause snoring than severe OSA. The degree of nasal obstruction and severity of SDB are in some studies not strongly associated (Olsen & Kern, 1990; Young et al, 1997b). In patients with allergic rhinitis, obstructive sleep apneas have a longer duration and increased frequency during periods of symptomatic nasal obstruction, and in habitual snoring
children, those with allergy had increased SDB (McNicholas et al, 1982; McColley et al, 1997). Treatment of nasal congestion resulted in subjective improvement in sleep quality, drop in nasal resistance and fewer arousals, but there was no significant improvement in sleep architecture, nocturnal oxygenation, or amount of apnea (Kerr et al, 1992a). Other studies have failed to demonstrate an association between nasal obstruction and SDB (Bloom et al, 1988; Miljeteig et al, 1993). On the other hand, experimentally provoked acute nasal obstruction caused a significant increase in obstructive respiratory events and sleep apnea developed in one subject on the basis of acute nasal obstruction . (Zwillich et al, 1981; Olsen et al, 1981).

Abnormalities of the upper airways

Skeletal anomalies such as midfacial hypoplasia, micrognathia, or deformation of the cranial base reduce the area of the upper airways, and predispose to snoring and sleep apnea. Correction of the structural abnormalities of the upper airways is likely to improve the patency and to reduce the number of sleep apneas (Johns et al, 1998; Isono et al, 1998; Hoeve et al, 1999). Adenotonsillar hypertrophy is a common cause of OSA in children, and may also induce sleep apnea in adult (Mangat et al, 1977; Shintani et al, 1998; Warwick & Mason, 1998).

Other related conditions that affect the upper airways are Marfan's and Down's syndrome. In Marfan's syndrome there is abnormally increased upper airway collapsibility during sleep, possibly related to the characteristic connective tissue defect (Cistulli & Sullivan, 1993; Cistulli & Sullivan, 1995). In Down's syndrome the upper airway obstruction is a more complex process with multifocal causes including both soft-tissue abnormalities including lymphoid hyperplasia or macroglossia, and skeletal deformities such as midface retrusion (Marcus et al, 1991; Ferri et al, 1997; Lefaivre et al, 1997; Levanon et al, 1999).

Obstructive pulmonary disease

The association between obstructive pulmonary diseases and OSA is still not clear with disagreement in results from different studies. Obstructive lung function impairment in OSA patients was found by some investigators (Zerah-Lancner et al, 1997; Appelberg et al, 2000), but some expert opinions
are that there is no evidence that chronic obstructive pulmonary disease (COPD) and snoring or OSA are related (Douglas & Flenley, 1990; Fett et al, 1991). Snoring appears to be linked to cough and wheeze (Bloom et al, 1988; Fitzpatrick et al, 1993; Honsberg et al, 1995). In a small sample Lin and Lin (1995) found bronchial hyperreactivity in 4 out of 16 patients with OSAS. BHR was unrelated to the severity of OSAS, but 3 months of CPAP therapy decreased hyperreactivity to methacholine. Janson et al (1996) reported higher prevalence of snoring and self-reported apneas in asthmatics compared with non-asthmatics, but could not find a strong association between bronchial hyperreactivity and snoring. In other studies patients with concomitant OSA and nocturnal asthma were improved during CPAP therapy with increase in peak expiratory flow, and less nocturnal asthma symptoms (Chan et al, 1988; Guilleminault et al, 1988b).

Endocrine disorders

Up to 75% of patients with acromegaly have sleep apnea (Weiss et al, 2000). There is an obstruction in the upper airways, due to hypertrophy of the tongue and pharyngeal tissues, that leads to snoring and OSA (Grunstein et al, 1994a). Patients with acromegaly also often suffer from central apneas (Grunstein et al, 1994b).

In hypothyroidism the associated edema and myopathy appear to be of pathogenic importance for OSA, especially when myxedema is present. Thyroxin substitution is often of benefit for reducing OSA in these patients (Orr et al, 1981; Grunstein, 1994).

The relation to diabetes mellitus is complex. Both OSA and diabetes share obesity as a common risk factor (Grunstein et al, 1995a). There is also reported independent association between snoring, OSA and diabetes (Strohl et al, 1994; Elmasry et al, 2000) or insulin resistance regardless of obesity (Tiihonen et al, 1993; Scheen & Van Cauter, 1998; Vgontzas et al, 2000). Diabetic neuropathy has been proposed as etiological factor for development of snoring (Rosenow et al, 1998).
The most important consequences of snoring and OSA are related to the influence on metabolic and cardiovascular factors, on sleepiness and cognitive function, and on social consequences as divorce (Grunstein et al, 1995b).

CARDIOVASCULAR CONSEQUENCES

Hypertension

Most studies have found an independent association between both snoring and OSA and arterial hypertension (Jenum & Sjol, 1993; Carlsson et al, 1994; Lindberg et al, 1998a; Peppard et al, 2000b; Bixler et al, 2000; Ohayon et al, 2000; Nieto et al, 2000; Grote et al, 2000). Both age and obesity are strong confounding factors. In almost every study arterial hypertension is associated with snoring, but after adjustment for risk from age and obesity, snoring and OSA are not always independently linked to high blood pressure (Gislason et al, 1987; Stradling & Crosby, 1990; Jennum & Sjol, 1992; Koskenvuo et al, 1994). Heart rate and blood pressure varies during the night in OSA, while normal subjects show a fall in blood pressure and a decrease in heart rate at sleep onset (Tilkian et al, 1976; Davies et al, 1994).

Coronary artery disease

OSA may predispose to cardiovascular disease by repeated hypoxia and sleep fragmentation probably mediated by sympathetic activation (Hedner et al, 1988; Hedner et al, 1995). A number of studies report an independent association between snoring, OSA and coronary artery disease (Smirne et al, 1993; Franklin et al, 1995; Mooe et al, 1996a; Mooe et al, 1996b; Schafer et al, 1999; Peker et al, 2000).
Cerebrovascular disease

Subjects with snoring or OSA have an increased risk for cerebral ischemia and stroke (Partinen & Palomäki, 1985; Spriggs et al, 1992; Smirne et al, 1993; Neau et al, 1995; Bassetti & Aldrich, 1999).

Arrhythmias

A high incidence of nocturnal cardiac rhythm disturbances among patients with obstructive sleep apnea syndrome has been described. Some investigators have found that OSA predisposes to clinically significant cardiac rhythm disturbances, heart block, and apnea-associated bradyarrhythmias (Koehler et al, 1991). The arrhythmias are possible due to an autonomic dysfunction of the parasympathetic system in patients with OSAS (Wiklund et al, 2000). The arrhythmias can often successfully be controlled by CPAP therapy (Koehler et al, 1998; Harbison et al, 2000). On the other hand, in a study on 246 subjects with disabling angina pectoris and verified coronary artery disease, serious arrhythmias were not found to be associated with sleep apnea (Mooe et al, 2000).

Pulmonary hypertension

Pulmonary arterial hypertension is often found in patients with OSA (Sajkov et al, 1994; Laks et al, 1995; Sanner et al, 1997; Sajkov et al, 1999). Though traditionally thought of associated with chronic obstructive pulmonary disease (COPD), the overlap syndrome (Tilkian et al, 1976; Krieger et al, 1989; Aprill et al, 1991; Chaouat et al, 1995; Kessler et al, 1996), pulmonary arterial hypertension is frequently observed in patients with OSA, even when COPD is absent, and appears to be related to the severity of obesity and its respiratory mechanical consequences (Podszus et al, 1986; Chaouat et al, 1996; Bady et al, 2000). In some patients with OSA, pulmonary artery pressure progressively increases during the night, reflecting the cumulative effects of apneas and nocturnal hypoxia, though if this increases mortality in otherwise healthy subjects is not known (Sforza et al, 1998). Patients with acute respiratory insufficiency due to COPD and OSA can be treated with CPAP. Although the acute effect usually is successful (Fletcher et al, 1991), patients with both OSA and COPD have an
increased mortality compared with patients who have OSA alone (Chaouat et al, 1999).

**DRIVING ACCIDENTS**

Patients with snoring or OSA have more traffic accidents than non-snoring, non-OSA subjects (Findley et al, 1988; Stoohs et al, 1994; Findley et al, 1995; Wu & Yan-Go, 1996; Barbé et al, 1998; Masa et al, 2000). Treatment with CPAP reduces the frequency of motor vehicle accidents (Cassel et al, 1996; Krieger et al, 1997; Yamamoto et al, 2000). Performance in a driving simulator is worse in subjects with obstructive sleep apnea than in control subjects, and the driving performance improves in subjects with OSA after treatment with nasal CPAP (Findley et al, 1989; George et al, 1997). In a sample of 913 men and women in a general working population, Young et al (1997a) found that men with AHI≥5, compared to those without sleep-disordered breathing, were significantly more likely to have at least one accident in 5 years. Subjects with AHI>15 had seven times increased risk for multiple traffic accidents in 5 years.

**OCCUPATIONAL ACCIDENTS**

The risk of being involved in an occupational accident was approximately 2-fold among male heavy snorers and increased by 50% among men suffering from obstructive sleep apnea syndrome in a retrospective study. For females the risk increased by at least 3-fold among heavy snorers and subjects with OSAS (Ulfberg et al, 1999).

**TREATMENT**

**CONTINUOUS POSITIVE AIRWAY PRESSURE**

CPAP is the most widely used treatment for severe OSAS. It was introduced by Sullivan et al (1981) and consists of a turbine or compressor that produces airflow with adjustable positive air pressure. This positive air pressure is transmitted to the patient's airways through a nasal mask. The
pressure acts as a pneumatic splint and prevents upper airway occlusion. It is important that the pressure is sufficient to keep the upper airways open (Jenkinson et al, 1999; Hack et al, 2000). The effect on both snoring and OSA is immediate. CPAP is an effective treatment of OSA and up to 80% of patients are compliant with the treatment (Pepin et al, 1999). Discomfort from the nose or pharynx and lack of subjective effect were the two most common reasons for non-compliance in a study of patients who were unable to tolerate CPAP treatment (Janson et al, 2000). CPAP is effective in reducing OSA related symptoms such as sleepiness, daytime somnolence, alertness, daytime dysfunctioning and cardiovascular consequences (Sforza et al, 1990; Hedner et al, 1995; Bolitscheck et al, 1998; Chaouat et al, 1999; Jenkinson et al, 1999; Hack et al, 2000).

SURGICAL THERAPY

Tracheostomy

Tracheostomy is the ultimate treatment for obstructive sleep apnea. It bypasses the collapsible parts of the upper airway (Kuhlo et al, 1969; Lugaresi et al, 1970), and is indicated in severe therapy-resistant OSA.

Nasal surgery

Nasal surgery, such as reconstruction of the nasal septa (Series et al, 1993), can be effective in relieving nasal symptoms and facilitate treatment with nasal CPAP, but it is seldom sufficient by itself for treatment of OSA (Friedman et al, 2000).

Uvulopalatopharyngoplasty

Uvulopalatopharyngoplasty (UPPP) was introduced by Fujita et al (1981). It was for many years a common treatment for snoring and mild OSA. Side effects as severe postoperative pain, nasal regurgitation, pharyngeal hypersecretion, swallowing problems, and speech disturbances are common
In selected patients with mild OSA or habitual snoring, UPPP has good long-term effect (Hultcrantz et al, 1999).

Maxillomandibular advancement

Maxillomandibular advancement is in selected patients an effective method to treat both snoring and OSA (Riley et al, 1986; Riley & Powell, 1990; Li et al, 2000b).

Radiofrequency

Radiofrequency therapy is used both for pacing of the muscle in the upper airway and for thermal ablation of upper airway tissues. Both methods have recently been introduced in the treatment of snoring and OSA, and there are no studies on long term outcome (Guilleminault et al, 2000). Radiofrequency volumetric tissue reduction has probably a higher relapse incidence than UPPP, but much less discomfort and postoperative pain. Radiofrequency volumetric tissue reduction can be administered as an outpatient procedure, but many applications are needed, and treatment may span 6 months (Guilleminault et al, 2000; Li et al, 2000a; Troell et al, 2000).

ORAL APPLIANCES

Specially designed oral appliances can be an effective treatment in selected patients (Ferguson et al, 1997; Liistro et al, 1998; Marklund et al, 1998a,b; Borgersen et al, 2000; Lowe et al, 2000), especially in patients with supine-dependent sleep apnea (Marklund et al, 1998c). Increasing the cross-sectional area of the airways in pharynx by moving the mandible and the tongue forward stabilises the upper airways. It improves upper airway obstruction and reduces snoring and OSA.
WEIGHT LOSS

Weight loss is associated with decreases in upper airway collapsibility in obstructive sleep apnea and there are several reports where weight loss after dietary regimen or weight reduction surgery has improved snoring and OSA (Schwartz et al., 1991; Rajala et al., 1991; Dixon et al., 2001). The Wisconsin study reported that clinical and public health programs with modest weight control reduction were effective. A 10% weight gain predicted an approximate 32% increase in the AHI, and a 10% weight loss predicted a 26% decrease in the AHI. A 10% increase in weight predicted a 6-fold increase in the odds of developing moderate to severe SDB (Peppard et al., 2000a).

SLEEPING POSITION

Some patients have snoring and apneas almost only when sleeping in a supine position. They can be treated with devices that prevent them from lying on their back or training to avoid supine position (Cartwright et al., 1991; Oksenberg et al., 1997). In patients with severe OSA who have a high number of apneic events in the supine and lateral posture, the apneic events occurring in the supine position are more severe than those occurring while sleeping in the lateral position (Oksenberg et al., 2000).

DRUGS

Both alcoholic beverages and sleeping pills should be avoided (Dolly & Block, 1982), since bedtime ethanol increases resistance of upper airways, and flurazepam has been associated with significant increases in the number of apneic events (Mitler et al., 1988; Jennum & Sjol, 1992; Scanlan et al., 2000).
NASAL DEVICES

Nasal-valve dilation reduces nasal resistance and increases airflow. There are different opinions about the procedure’s effectiveness. Some claim that at least some patients get a reduction in their snoring (Pevernagie et al, 2000), but without effect on arousals or EDS (Hoijer et al, 1992), while other report that these devices have no effect on either snoring nor SDB (Liistro et al, 1998; Schonhofer et al, 2000).
AIMS OF THE STUDY

The overall aims with this thesis were to explore occurrence of symptoms related to obstructive sleep apnea in Norrbotten, and their relation to other respiratory disorders.

Specific aims were the following:

- to study if snoring as a problem, relatives' concern about witnessed apnea, and symptoms of daytime sleepiness are related to bronchitic symptoms.

- to investigate if snoring as a problem, relatives' concern about witnessed apnea, and symptoms of daytime sleepiness are related to lung function impairment.

- to assess to what extent snoring as a problem reflects OSA and OSAS.

- to study if the prevalence of OSA is higher in subjects with bronchitic symptoms than in subjects without respiratory complaints.

- to study if snoring as a problem, relatives' concern about witnessed sleep apnea, and symptoms of daytime sleepiness are related to respiratory symptoms, asthma, and rhinitis.

- to identify risk factors, including gender differences and the influence of smoking, for snoring as a problem, relatives' concern about witnessed sleep apnea, and daytime sleepiness.

- to investigate the relation between the number of subjects with OSA symptoms and the number of all subjects who actually have been referred to sleep lab.
METHODS

STUDY AREA

Norrbotten is the northernmost part of Sweden with a population of 256,000 inhabitants (31 Dec 2000, Statistics Sweden). Norrbotten comprises 24% of the area of Sweden, but has only 3% of the population. It is thus a sparsely inhabited region with a large mountainous area in the inland and most people living in the coastal districts.

STUDY DESIGN

In 1991 a questionnaire was sent by mail to subjects, previously identified as having bronchitis or to be without respiratory disease (paper I). The questionnaire was followed by a structured interview and lung function tests 1992 (paper II). A validation study based on sleep studies was performed in 1994-95 in subjects with snoring as a problem in the questionnaire study (paper III).

A second questionnaire was in 1992 sent to a representative sample of the general population (paper IV and V). In paper V the results from the questionnaire survey were also analysed in relation to all patients referred to sleep lab between 1990 - 2000.

STUDY POPULATION

Two cohorts and one patient sample have been investigated in the studies in this thesis (Fig 1).

The first study cohort was derived from the first of the Obstructive Lung Disease In Northern Sweden Studies (OLIN) in 1986, where all 6,610 subjects born 1919-20, 1934-35 and 1949-50 in representative geographical areas in Norrbotten were assessed concerning airway diseases. The study sample consisted of two groups; a bronchitic group comprising all subjects who had reported bronchitic disease, and a reference group with a stratified
sample of subjects without respiratory complaints in the 1986-year study (paper I-III) (Table 1.).

Table 1. Participants by age, gender, and smoking habits in the bronchitic and the reference groups, respectively.

<table>
<thead>
<tr>
<th>Age cohort</th>
<th>1919 - 1920</th>
<th>1934 - 1935</th>
<th>1949 - 1950</th>
<th>All</th>
<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
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<tr>
<td>71 - 72 y</td>
<td>(101) (89)</td>
<td>(64) (90)</td>
<td>(115) (84)</td>
<td>(63) (86)</td>
<td>(63) (77)</td>
</tr>
<tr>
<td>41 - 42 y</td>
<td>(56) (35)</td>
<td>(41) (26)</td>
<td>(52) (64)</td>
<td>(70) (77)</td>
<td>(50) (77)</td>
</tr>
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</table>

The study sample in paper II included responders from the study population in the paper I study and comprised 579 of 736 invited subjects (79%). The subjects were divided in three groups. A bronchitic group, with 357 of 450 subjects, 79% of all responders from the bronchitic group in the paper I study. A random sample (RR group), after stratification for age and sex, 140 of 178 invited subjects (79%) from the reference group, and a symptomatic reference group (RS group), with 82 of 108 subjects (76%) that reported symptoms of bronchitis in the reference group in the paper I study and not were included in the RR group.

The study sample in paper III consisted of 52 of 70 invited subjects (74%) expressing snoring to be a problem in the paper I study.
The second study population, described in paper IV-V, consisted of 4,648 subjects, 85.7% of invited 5,424 of all 5,682 subjects aged 20-69 years, born on the 15th day of each month and living in the province (Table 2).

Table 2. Invited and participated subjects by age and gender.

<table>
<thead>
<tr>
<th></th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>All</th>
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<tr>
<td>In Men</td>
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<tr>
<td>Invited</td>
<td>588</td>
<td>525</td>
<td>645</td>
<td>626</td>
<td>534</td>
<td>485</td>
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<tr>
<td>(%)</td>
<td>(81)</td>
<td>(88)</td>
<td>(81)</td>
<td>(89)</td>
<td>(86)</td>
<td>(93)</td>
</tr>
<tr>
<td>Participated</td>
<td>478</td>
<td>462</td>
<td>524</td>
<td>541</td>
<td>497</td>
<td>421</td>
</tr>
<tr>
<td>(%)</td>
<td>(81)</td>
<td>(88)</td>
<td>(81)</td>
<td>(89)</td>
<td>(86)</td>
<td>(93)</td>
</tr>
</tbody>
</table>

In men, 29% reported that they were current smokers, 24% were ex-smokers. In women, 32% were current smokers, and 16% ex-smokers. Smoking habits are shown in Figure 1.

Figure 1. Smoking habits (%) by gender and age.

The patient sample in paper IV consisted of all 4,188 patients in corresponding age referred to Sunderby hospital for sleep studies to evaluate suspected OSA.
Figure 2. Study design and participants.

- **Population sample (6610)**
  - **Paper I**
    - **Bronchitic group (450)**
      - 86% of invited
    - **Reference group (529)**
      - 85% of invited

- **Paper II**
  - **Bronchitic group (357)**
    - 79% of invited
  - **Symptomatic reference group (82)**
    - 76% of invited
  - **Random reference group (140)**
    - 79% of invited

- **Paper III**
  - Snoring as a problem (52)
    - 74%

- **Paper IV**
  - **86% of invited (4648)**

- **Paper V**
  - **4648**
  - **4188**
    - Referred
The questionnaire was developed by Lundbäck for the OLIN studies (Lundbäck et al, 1991). It is a revised version (Stjernberg, 1985) of the MRC questionnaire (Medical Research Council's Committee, 1960) with influences from the ATS (Ferris, 1978), and the Tucson studies questionnaires (Lebowitz et al, 1975). The questionnaire has frequently been used in Nordic countries (Larsson, 1995; Lundbäck, 1998; Montnemery et al, 1998; Pallasaho et al, 1999; Rönmark et al, 1999; Kotaniemi et al, 2001), and has previously been validated (Lundbäck, 1993; Larsson, 1995). The questionnaire included questions about asthma, rhinitis, chronic bronchitis, and respiratory symptoms such as sputum production, long-standing cough, recurrent wheeze, and attacks of shortness of breath. It also included questions about profession, smoking habits, and use of asthma medicines.

Four questions related to obstructive sleep apnea were added to this questionnaire.

- Do you snore so much that you think it is a problem?
- Have relatives expressed worry about you stopping breathing while you are asleep?
- Do you feel completely rested after a full nights sleep?
- Do you nod off during breaks in daytime activities?

**CLINICAL INVESTIGATIONS**

The structured interview and lung function tests were executed by specially trained nurse (Lundbäck, 1993). The interview questionnaire was developed by Lundbäck from an expanded Swedish questionnaire (Stjernberg, 1985) for the OLIN studies (Lundbäck, 1993). The main parts of the questionnaire have later been used in comparative studies between Finland, Estonia, and Sweden (the FinEsS studies) (Pallasaho et al, 1999; Kotaniemi et al, 2001; Lindström et al, 2001).
The lung function tests were performed using a dry spirometer, Mijnhardt Vicatest 5, without nose clip and with the subjects standing, otherwise following the ATS recommendations (American Thoracic Society, 1979). Predicted values were taken from the Berglund normal values (Berglund et al, 1963).

DETERMINANTS OF DISEASE AND DIAGNOSTIC CRITERIA IN RESPIRATORY DISORDERS AND DISEASES.

The following questions about respiratory symptoms and conditions were used in the different studies.

**Recurrent wheeze**: "Yes" to the question "Do you usually have wheezing, whistling, or a noisy sound in your chest when breathing?"

**Long-standing cough**: "Yes" to the question "Have you had longstanding cough during the last years?"

**Attacks of shortness of breath**: "Yes" to the question "Do you now have, or have you had asthma symptoms (intermittent breathlessness or attacks of shortness of breath; the symptoms may exist simultaneous with or without cough or wheezing)?"

**Sputum production**: "Yes" to the question "Do you usually have phlegm when coughing, or do you have phlegm in your chest which is difficult to bring up?"

**Chronic productive cough**: "Yes" to the question "Do you usually have phlegm when coughing, or do you have phlegm, in your chest, which is difficult to bring up during periods of at least three month and have you had such periods during at least two successive years?"

**Physician-diagnosed asthma**: "Yes" to the question "Have you been diagnosed by a physician as having asthma?"

**Rhinitis**: "Yes" to the question "Do you have or have you ever had allergic eye-/nose catarrh (hay-fever)?"
SLEEP STUDIES

Overnight sleep apnea recordings were made at home. The recordings were sampled in MicroDigitrapper SAS (Synectics AB, Stockholm, Sweden). They included nasal and oral airflow assessed with a 3-port thermistor, respiratory and body movements using a pressure-sensitive bed, oxygen saturation (SaO₂) and heart rate by finger oxymetry, snoring registered with a microphone placed on the throat, and body position. The home-based polysomnography has previously been validated by Zucconi et al (1996). All recordings were manually scored and blinded regarding bronchitic symptoms.

An apnea was defined as a cessation of airflow for at least 10 s. A hypopnea was defined as an event when the airflow was markedly reduced with a concomitant oxygen desaturation of 4% or more (Guilleminault et al, 1976; Gould et al, 1988). Sleep duration was estimated from body movements, snoring sounds, periodic breathing, and from the subjects’ own information (Svanborg et al, 1990; Redline et al, 1991). The apnea hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of estimated sleep (Gould et al, 1988).

ANALYSES AND STATISTICAL METHODS

Statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS). Bi-variate comparisons were performed by Chi-square test and one way analysis of variance (ANOVA). FEV₁ percent of predicted in paper II was analysed in relation to bronchitic and OSAS-related symptoms in the whole study population. Fisher's two-tailed exact test was used to analyse differences between OSAS symptoms in subjects with different bronchitic symptoms in paper II. Linear regression analysis was used to calculate correlation between continuous variables and the results are presented as a standard coefficient of regression (r). For analysis of difference in ratios, z-test was used.
To assess the simultaneous influences of different independent variables, multiple logistic regression analysis was used, and the results are presented as the adjusted odds ratio (OR) with 95% confidence intervals (95% CI). The null hypothesis was rejected at the 5% level (p<0.05).

**ETHICAL ASPECTS**

The studies were approved by the Ethics Committee at Umeå University.
RESULTS

BRONCHITIC COHORT STUDIES (Papers I - III)

Analysis of the prevalence of snoring as a problem, relatives’ concern about witnessed apnea, not being rested after a full nights sleep, and tendency to nod off in the daytime in relation to bronchitic symptoms was the main aim of the first questionnaire study (Paper I).

The most common bronchitic symptom, sputum production, was reported by 53.3% in the bronchitic group and by 17.8% in the reference group. Corresponding figures for recurrent wheeze were 53.3% vs. 9.8%, long-standing cough 48.9% vs. 13.4% and for shortness of breath 38.2% vs. 8.1% respectively.

Compared with the reference group, all symptoms related with OSA were more prevalent in the bronchitic group as shown in Figure 3.

Figure 3. Prevalence of snoring as a problem, relatives’ concern about witnessed apnea, not rested after a full nights sleep, and tendency to nod off in the daytime in the bronchitic and reference groups, respectively.
The main aim with the second study was to investigate if symptoms of OSA were related with bronchitic symptoms, lung function impairment, or both (Paper II). In the bronchitic group 357 subjects, 79% of all who received questionnaire, participated. Corresponding figures for the random reference group were 140 subjects (79%), and for the symptomatic reference group 82 subjects (76%).

The relation between bronchitic symptoms, which were long-standing cough, sputum production, recurrent wheeze and symptoms related with OSA, BMI and FEV$_1$ percent predicted is shown in Table 3. Snoring as a problem, relatives’ concern about witnessed sleep apnea, not rested and tendency to nod off were all significantly more common in subjects with complaints of sputum production, chronic productive cough, recurrent wheeze and at least one bronchitic symptom. Snoring, not rested, and tendency to nod off were also correlated with long-standing cough, while BMI was significantly higher in subjects with chronic productive cough and recurrent wheeze. FEV$_1$ was significantly lower in subjects reporting any of the bronchitic symptoms.

Table 3. Relationship between respiratory symptoms and symptoms expressing sleep disturbances (percent), BMI (kg/m$^2$) and FEV$_1$ (% of predicted), in subjects with and without bronchitic symptoms.

<table>
<thead>
<tr>
<th></th>
<th>Bronchitic symptoms</th>
<th>Snoring</th>
<th>Apnea</th>
<th>Not rested</th>
<th>Nod off</th>
<th>BMI</th>
<th>FEV$_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-standing cough</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17.5</td>
<td>13.3</td>
<td>28.7</td>
<td>9.4</td>
<td>25.6</td>
<td>91.0</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.4</td>
<td>8.3</td>
<td>20.1</td>
<td>3.5</td>
<td>25.1</td>
<td>98.3</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.044</td>
<td>0.111</td>
<td>0.043</td>
<td>0.022</td>
<td>0.157</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Sputum production</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>18.2</td>
<td>14.1</td>
<td>30.7</td>
<td>11.5</td>
<td>25.7</td>
<td>90.4</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.8</td>
<td>8.2</td>
<td>18.5</td>
<td>1.0</td>
<td>25.1</td>
<td>97.5</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.02</td>
<td>0.04</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td>0.070</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Chronic productive cough</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19.8</td>
<td>16.3</td>
<td>31.0</td>
<td>12.5</td>
<td>25.8</td>
<td>89.2</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.9</td>
<td>7.1</td>
<td>21.4</td>
<td>2.6</td>
<td>25.1</td>
<td>96.9</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.004</td>
<td>&lt;0.001</td>
<td>0.009</td>
<td>&lt;0.001</td>
<td>0.017</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Recurrent wheeze</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20.1</td>
<td>16.3</td>
<td>31.0</td>
<td>11.2</td>
<td>25.9</td>
<td>88.2</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.5</td>
<td>7.1</td>
<td>21.4</td>
<td>4.1</td>
<td>25.0</td>
<td>98.3</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td>0.009</td>
<td>0.002</td>
<td>0.004</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>At least one bronchitic symptom</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17.6</td>
<td>13.4</td>
<td>28.5</td>
<td>9.3</td>
<td>25.6</td>
<td>91.2</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7.4</td>
<td>6.5</td>
<td>18.5</td>
<td>1.9</td>
<td>25.2</td>
<td>99.8</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.009</td>
<td>0.05</td>
<td>0.04</td>
<td>0.009</td>
<td>0.445</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
BMI was slightly, but significantly, higher in subjects reporting snoring as a problem (26.5±4.1 vs. 25.3±3.6 in non-snorers, p=0.004), relatives’ concern about witnessed sleep apnea (26.7±3.9 vs. 25.3±3.7, p=0.004), and tendency to nod off (27.1±4.3 vs. 25.4±3.6, p=0.003). These results were similar among both men and women. There was no difference in BMI in subjects reporting not rested after a full nights sleep. No differences were seen in FEV₁ percent predicted or FVC percent predicted in subjects reporting sleep disturbances.

Multiple logistic regression analysis was performed for relations between bronchitic symptoms, BMI with a cut off level of 28, gender, ageclass, FEV₁ percent predicted with cut off level of 80% and smoking habits in the model. Snoring as a problem was independently correlated with bronchitic symptoms and ageclass 56-57 years old. Relatives’ concern about witnessed sleep apnea was correlated with bronchitic symptoms and male gender. Relatives’ concern about sleep apnea and snoring as a problem were included in the model when not rested and tendency to nod off were analysed. Not rested was independently associated with relatives’ concern about sleep apnea and snoring as a problem. Tendency to nod off was related to snoring and bronchitic symptoms.

In the third of the bronchitic cohort studies, the main aim was to assess to what extent reported snoring as a problem reflected OSA, and if the prevalence of OSA was higher in subjects with bronchitic symptoms (Paper III). Of the 91 subjects who had reported snoring as a problem, 70 were still alive and living within 250 km from the clinic. These were invited for a sleep study. Acceptable in-home sleep recordings were obtained from 52 subjects (74%) . Of these 52 subjects, 6 were free from respiratory symptoms.

Mean AHI was 15.4 ± 14.9 events/h and mean nadir SaO₂ was 82.3 ± 9.0%. There was a strong negative association between the lowest SaO₂ and AHI; r = 0.74 (p<0.001).

In this relatively small sample, only the age-class 61-62 years was independently associated with AHI analysed by using multiple logistic regression. Other independent variables included in the model were gender, smoking habits, FEV₁ percent predicted, and BMI. Apnea, in addition to snoring, was independently associated with AHI (Table 4).
Table 4. Associations between AHI ≥ 5, AHI ≥ 10, and AHI ≥ 15, and the symptoms relatives' concern about witnessed apnea, not rested after a night's sleep, and tendency to nod off during the daytime in subjects with snoring as a problem.

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Dependent Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>AHI ≥5</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
</tr>
<tr>
<td>Apnea n=59</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>9.66 (4.59-20.3)</td>
</tr>
<tr>
<td>Not rested n=102</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>2.84 (1.31-6.08)</td>
</tr>
<tr>
<td>Nod off n=35</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>1.34 (0.46-3.89)</td>
</tr>
</tbody>
</table>

Of the subjects with snoring as a problem, AHI ≥ 10 was found among 18% in the age-group 46-47 y, 60% among the subjects 61-62 y, and in 64% in the oldest age-group, 76-77 y. The corresponding figures for AHI ≥ 10 with daytime sleepiness were 9%, 40%, and 27%.

Based on the prevalence rates of snoring and daytime symptoms in the two groups, prevalence rates for AHI and AHI with concomitant daytime symptoms were calculated. As shown in Table 5, prevalence rates for AHI at different cut off levels were twice as high in bronchitics as in respiratory healthy subjects.

Table 5. Calculated prevalence rates (%) of AHI in subjects with bronchitic and respiratory healthy subjects, respectively (n=579).

<table>
<thead>
<tr>
<th></th>
<th>AHI ≥ 5</th>
<th>AHI ≥ 10</th>
<th>AHI ≥ 15</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With</td>
<td>With</td>
<td>With</td>
</tr>
<tr>
<td></td>
<td>Symptoms*</td>
<td>Symptoms*</td>
<td>Symptoms*</td>
</tr>
<tr>
<td>Subjects with bronchitis</td>
<td>13.5</td>
<td>9.1</td>
<td>6.8</td>
</tr>
<tr>
<td>Respiratory healthy subjects</td>
<td>5.7</td>
<td>3.8</td>
<td>2.8</td>
</tr>
</tbody>
</table>

* Either not rested after a night's sleep and/or nod off during the daytime.
The main aim in the general population studies was to explore symptoms related to OSA in a general population and to examine their relation with respiratory conditions and other possible risk factors. A further aim was to analyse the relationship of referral for sleep studies with the estimated number of subjects with snoring and apneas in Norrbotten.

Physician diagnosed asthma was reported by 6.6% of men and by 7.6% of women. The prevalence of recurrent wheeze was 12.1% in men and 11.5% in women. Chronic productive cough was reported by 7.6% of men and 6.7% of women, and increased significantly by age. The prevalence of rhinitis decreased with increasing age, and was overall 18.5% in men and 20.4% in women.

To have snoring as a problem was reported by 10.7% (men 14.6%, women 6.7%, p<0.001). In men there was a peak prevalence in the age-group 55-59 years, and in women in age-group 60-64 years (Figure 4).

Figure 4. Prevalence (%) of snoring as a problem in men and women by age.
Relatives' concern about witnessed sleep apnea was reported by 6.8%. The gender difference was greater than for snoring. 11.0% of men and 2.4% of women (p<0.001) reported witnessed apneas (Figure 5).

Figure 5. Prevalence (%) of reported concern about witnessed sleep apnea in men and women by age.

Not being rested after a full nights sleep was reported by 26.0% of men and by 24.7% of women (p=0.323). Tendency to nod off was significantly more common among men, 6.9% vs. 5.3% among women (p=0.023). At least one of the two daytime symptoms, not rested or tendency to nod off, were reported equally prevalent among men and women, 29.4% vs. 27.2%, respectively (p=0.098). There was a gender difference in reporting daytime symptoms concomitant with reporting snoring as a problem. Women who had snoring as a problem reported either of the two daytime sleepiness symptoms in 58%, men in 48% (p=0.031). In contrast to prevalence rates in the whole group, snoring women reported each of the daytime symptoms more often than snoring men did. Not rested was reported by 50.3% of
snoring women and by 40.4% of snoring men (p=0.039). Corresponding figures for tendency to nod off was 23.5% vs. 20.3% (p=0.424).

Both snoring as a problem and relatives’ concern about witnessed apnea were reported more commonly in subjects who also reported bronchitis, physician diagnosed asthma, recurrent wheeze, or rhinitis (Table 6).

Table 6. The prevalence (%) of snoring as a problem and relatives’ concern about witnessed apnea in relation to smoking habits and airway conditions in men (M) and women (W), respectively.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Snoring as a problem</th>
<th>Concern about apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Non smokers</td>
<td>10.4</td>
<td>6.2</td>
</tr>
<tr>
<td>Ex smokers</td>
<td>16.5</td>
<td>6.4</td>
</tr>
<tr>
<td>Current smokers</td>
<td>20.1</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Chronic Bronchitis</td>
<td>31.5</td>
<td>18.8</td>
</tr>
<tr>
<td>No</td>
<td>13.3</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Physician diagnosed asthma</td>
<td>21.9</td>
<td>14.4</td>
</tr>
<tr>
<td>No</td>
<td>14.1</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.008</td>
</tr>
<tr>
<td>Wheezing</td>
<td>28.1</td>
<td>14.0</td>
</tr>
<tr>
<td>No</td>
<td>12.8</td>
<td>5.7</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>20.0</td>
<td>9.8</td>
</tr>
<tr>
<td>No</td>
<td>13.4</td>
<td>5.9</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The relationship of snoring as a problem, the combination of snoring and daytime sleepiness, and relatives’ concern about witnessed apnea during sleep to age, gender, smoking habits, and different respiratory symptoms and diseases was analysed by using multiple logistic regression.

Age, male gender, chronic bronchitis, physician-diagnosed asthma, rhinitis, and current smoking were significantly related to snoring as a problem and
also to the combination of snoring and daytime sleepiness. When recurrent
wheeze was included in the analysis, physician-diagnosed asthma no longer
was significant, and instead of asthma, recurrent wheeze was significantly
related with snoring and with the combination of snoring as a problem and
daytime sleepiness. Age, male gender, recurrent wheeze, chronic bronchitis,
physician-diagnosed asthma, rhinitis, and current smoking were all
significantly associated with relatives' concern about witnessed apnea during
sleep (Table 7).

Table 7. Risks (OR and 95% CI) for snoring as a problem, relatives' concern
about witnessed apneas, and daytime sleepiness, respectively, by
multiple logistic regression analysis.

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Snoring</th>
<th>Apneas</th>
<th>Daytime sleepiness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Women</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Men</td>
<td>2.57 (2.09-3.17)</td>
<td>5.48 (4.05-7.43)</td>
<td>0.97 (0.84-1.11)</td>
</tr>
<tr>
<td>20-29</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>30-39</td>
<td>2.86 (1.85-4.40)</td>
<td>1.37 (0.80-2.33)</td>
<td>1.06 (0.86-1.30)</td>
</tr>
<tr>
<td>40-49</td>
<td>5.12 (3.38-7.75)</td>
<td>1.16 (0.94-1.44)</td>
<td>1.14 (0.92-1.43)</td>
</tr>
<tr>
<td>50-59</td>
<td>6.48 (4.25-9.86)</td>
<td>5.31 (3.28-8.60)</td>
<td>1.15 (0.92-1.44)</td>
</tr>
<tr>
<td>60-69</td>
<td>4.37 (2.82-6.77)</td>
<td>4.19 (2.55-6.90)</td>
<td>1.15 (0.92-1.44)</td>
</tr>
<tr>
<td>Non smokers</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ex smokers</td>
<td>1.13 (0.87-1.46)</td>
<td>1.09 (0.91-1.30)</td>
<td>1.17 (1.01-1.37)</td>
</tr>
<tr>
<td>Smokers</td>
<td>1.55 (1.24-1.94)</td>
<td>1.98 (1.49-2.62)</td>
<td>1.17 (1.01-1.37)</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>2.40 (1.80-3.20)</td>
<td>2.39 (1.70-3.35)</td>
<td>2.02 (1.59-2.57)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.62 (1.16-2.27)</td>
<td>2.36 (1.60-3.48)</td>
<td>1.17 (0.91-1.52)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>1.77 (1.40-2.24)</td>
<td>1.63 (1.21-2.20)</td>
<td>1.21 (1.02-1.44)</td>
</tr>
<tr>
<td>Snoring</td>
<td>-</td>
<td>-</td>
<td>1.85 (1.47-2.32)</td>
</tr>
<tr>
<td>Apneas</td>
<td>-</td>
<td>-</td>
<td>2.30 (1.73-3.04)</td>
</tr>
</tbody>
</table>

By using multiple logistic regression analysis, subjects with higher
education, or self employed reported snoring as a problem more often than
non-manual and manual workers in industry and service (OR 1.28 95% CI
1.02-1.60). Adjustment was made for gender, ageclass and smoking habits.
REFERRAL TO SLEEP CLINIC

Between 1990 and 2000, 3,955 patients, 2,991 men and 964 women, 20-69 years old had been referred to sleep lab. The association between referred patients and estimated numbers of subjects with snoring as a problem or relatives’ concern about witnessed apnea was analysed. Men reported snoring as a problem or relatives’ concern about witnessed apnea 2.9 times more often than women did. Adjusted for gender differences in the population, admission notes to sleep lab had a man/woman ratio of 3.1. When admission rates were compared with prevalence of snoring as a problem or relatives’ concern about witnessed apnea, men were referred to sleep lab 1.25 times more often than women. Age differences in reference rates are shown in Table 8.

Table 8. Prevalence of snoring as a problem or witnessed apneas, subjects referred to sleep lab 1990-2000 in percent of the population, by age and gender. Ratio percent referred in relation to population / prevalence snoring or apneas in the population.

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>20-69</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snoring as a problem</td>
<td>2.8</td>
<td>5.9</td>
<td>8.2</td>
<td>10.6</td>
<td>10.1</td>
<td>7.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Or witnessed apneas</td>
<td>6.5</td>
<td>13.5</td>
<td>22.7</td>
<td>29.2</td>
<td>19.2</td>
<td>17.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>p-value</td>
<td>0.008</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.008</td>
</tr>
</tbody>
</table>

| Age     | Men     | 1.0 | 2.7 | 5.1 | 4.9 | 3.3 | 3.5 |
| Referred to sleep lab | 0.3 | 0.9 | 1.6 | 1.8 | 1.3 | 1.2 |
| p-value | NS | NS | NS | NS | NS | NS | 0.012 |

| Age     | Men     | 0.15 | 0.20 | 0.22 | 0.17 | 0.17 | 0.20 |
| Ratio Referred : Snoring as a problem or witnessed apneas | 0.11 | 0.15 | 0.20 | 0.17 | 0.13 | 0.16 |
| p-value | NS | NS | NS | NS | NS | NS | 0.012 |
DISCUSSION OF METHODOLOGY

BACKGROUND

The studies in this thesis were planned in the early 90's. At that time one of our main interest was the overlap syndrome, the combination of OSA and chronic obstructive pulmonary disease that had been described a few years earlier (Flenley, 1985). Most studies examining the relation between snoring, OSA and lung function, COPD, or respiratory symptoms, were performed in sleep clinic patients and not in subjects without obvious history of snoring or suspected OSA (Fletcher, 1990; Fett et al, 1991) but the first reports from Tucson epidemiological study of obstructive airways disease indicated that presence of cough or sputum production was associated with an increase in snoring prevalence especially in ex-smokers (Bloom et al, 1988).

The ongoing OLIN-studies provided the opportunity to examine snoring and other symptoms of OSA in a large cohort with various bronchitic symptoms, and to relate these symptoms to lung function and clinical findings.

STUDY SAMPLE

Studies that examine variables with low prevalence require a large number of participants, and the strength of the studies in this thesis is the large study samples. Further, the samples of subjects with airway disorders are well defined (Lundbäck et al, 1991; Lundbäck et al, 1993; Lundbäck et al, 1994; Rönmark et al, 1999).

QUESTIONNAIRES AND DETERMINANTS OF DISEASE

THE OLIN QUESTIONNAIRE

It is important that a questionnaire is validated in the population where it will be employed (Brogger et al, 2000). In the current studies it was the original
OLIN questionnaire that has been validated (Lundbäck et al, 1994) and used in two Swedish dissertations (Lundbäck, 1993; Larsson, 1995; Rönmark, 1999) as well as in other studies in Nordic and Baltic countries (Montnemery et al, 1998; Pallasaho et al, 1999; Kotaniemi et al, 2001).

RESPIRATORY DISORDERS

How to define asthma in epidemiological studies has been discussed (Samet, 1987; Pride, 1989). There are no simple tests or measures that ensure correct diagnosis. We have therefore chosen physician diagnosed asthma, which is a diagnosis that is established through many different investigations, and has been shown to generally have a high specificity (Toren et al, 1993), which confirms well also with the results found in studies in Northern Sweden (Lundbäck, 1993; Larsson, 1995; Rönmark, 1999). Reporting chronic productive cough in a questionnaire is a better measure than physician diagnosed chronic bronchitis, since chronic bronchitis diagnosed by physician strongly underestimates the real occurrence of the disease (Ohlsson et al, 1984; Lundbäck, 1993).

Subjects reporting recurrent wheeze have an obstructive pulmonary disorder. Recurrent wheeze has a high specificity for obstructive pulmonary disease, however it cannot discriminate between asthma and chronic bronchitis (Lundbäck et al, 1991; Lundbäck et al, 1994; Larsson, 1995).

Another item that we used from the questionnaire was long standing cough. This symptom is less specific and does not unequivocally indicate chronic disease. Cough is also sensitive for common cold and other upper airway infections.

The question about rhinitis in the questionnaire was presumed to be more related to allergy, current or past, and not sensitive for ongoing rhinitis. This may weakens the ability of the questionnaire to identify the relationship of reported rhinitis to snoring.

SYMPTOMS RELATED TO OSAS

Four questions related to OSA were added to this questionnaire. The question about snoring as a problem was chosen in order to identify subjects who have so much snoring that they possible could seek medical advice. This gives perhaps more specific clinical information about snoring and could probably provide a better idea of the demand for sleep investigations.
than to use the frequency of snoring alone. On the other hand, it makes it difficult to compare the results with results from other studies using the frequency of snoring, defined as snoring every or almost every night. Regarding apneas, our aim was to identify subjects whose breathing pauses during sleep were so pronounced that it frighten their relatives. Apneas can occur without upper airway obstruction as for example in central apneas. Thus, in order to identify subjects in need of sleep apnea investigations, we have to include also subjects with sleep apneas that doesn’t snore. A confounding factor could be different awareness of breathing pauses. It is possible that relatives’ of subjects with airway diseases as asthma or chronic bronchitis are more prone to register breathing irregularities or breathing pauses.

The question about daytime sleepiness is somewhat nonspecific since it is difficult to quantify sleepiness. The test that has been referred to as a reliable reference test that estimate somnolence has been the MSLT. In questionnaires, questions about being refreshed after a night’s sleep or to have tendency to nod off during breaks in activity in the daytime have been used (Gislason et al, 1987; Petiau et al, 1993; Lindberg et al, 1998b), or, as in the Epworth Sleepiness Scale, a hypothetical estimation of dozing off in various situations (Johns, 1994). The questions about sleepiness in the current studies are almost the same as those used in other Swedish studies (Gislason et al, 1988; Lindberg et al, 1998c) except for grading yes / no instead of a 5 point scale.

In the validation study, a portable sleep apnea monitoring device was used. There are several studies reporting that in-home monitoring with portable device provides a valid and highly reproducible index for assessment of sleep-related respiratory disturbances for use in epidemiological studies (Redline et al, 1991; Van Surell et al, 1995; Man & Kang, 1995; Zucconi et al, 1996; Mykytyn et al, 1999; Fletcher et al, 2000; Vazquez et al, 2000). Although the recording program has an automated scoring system, the recordings were manually scored in order to improve both specificity and sensitivity (Zucconi et al, 1996). The main difficulties are to estimate sleep time and to assess hypopneas.

Svanborg et al (1990) found a good but not absolute agreement between the sleep time estimated by a static charge sensitive bed and from EEG, and Franklin and Svanborg (2000) found that subjects estimation of sleeping time was better predictor of EEG sleeping time than time in bed. We
estimated sleep time by a combination of information from the static charge sensitive bed, the oxymetry and from the subjective sleep estimation. The difference between estimated sleep time and registered time was small in the present studies.
DISCUSSION OF MAIN RESULTS

The main findings of the present studies were that problem with snoring and relatives’ concern about witnessed sleep apnea are more commonly reported by subjects with chronic bronchitis, asthma, rhinitis, and also by current smokers, but not by subjects with lung function impairment. Further, compared with the respiratory healthy, the obstructive sleep apnea syndrome is more common in subjects with bronchitis. Women with snoring as a problem complain more often of daytime sleepiness than men with snoring as a problem. Compared to men, women with snoring as a problem or witnessed sleep apnea were over the last decade referred significantly less often to sleep studies though they report more daytime sleepiness symptoms.

SYMPTOMS RELATED TO OSA

Snoring as a problem

The prevalence of the symptoms related to OSA was almost the same in the two questionnaire studies (Paper I, Paper V). Men reported snoring as a problem twice as often as women, similar to other reports of habitual snoring (Jennum & Sjol, 1992; Young et al, 1993; Ohayon et al, 1997; Neven et al, 1998). The difference in snoring prevalence between studies is large, and snoring as a problem in our study was reported less frequently than habitual snoring in other studies. This difference is probably due to difference in the definition of snoring. Other studies include subjects with snoring who not necessarily regard their snoring to be a problem. In Table 9, a summery of epidemiological studies on snoring is presented. As found by others, reported snoring increased with age in men with a highest prevalence in those aged 55-59 years (Honsberg et al, 1995; Lindberg et al, 1998c). Few women had snoring as a problem until the age of 55 when there was a doubling of reported snoring. It appears that menopause can be responsible for the rise in reported snoring in women in that age (Shaver & Zenk, 2000), and therapy with progestin and estrogen have given divergent results. Some studies have found a protective effect with decreased
<table>
<thead>
<tr>
<th>Author</th>
<th>Study place</th>
<th>Participants</th>
<th>Age</th>
<th>Definition of snoring</th>
<th>Prevalence snoring %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gislason et al, 1988</td>
<td>Uppsala Sweden</td>
<td>3100 M</td>
<td>30-69</td>
<td>Often or very often</td>
<td>15.6 M</td>
</tr>
<tr>
<td>Jennum &amp; Sjol, 1992</td>
<td>Copenhagen Denmark</td>
<td>728 M</td>
<td>30-60</td>
<td>6-7 times a week</td>
<td>19.1 M 7.9 F</td>
</tr>
<tr>
<td>Young et al, 1993</td>
<td>Wisconsin USA</td>
<td>1670 M</td>
<td>30-60</td>
<td>Every or almost every night</td>
<td>44 M 28 F</td>
</tr>
<tr>
<td>Ferini-Strambi et al, 1994</td>
<td>Milan Italy</td>
<td>349 M</td>
<td>40-65</td>
<td>Always</td>
<td>17 M</td>
</tr>
<tr>
<td>Honsberg et al, 1995</td>
<td>Tucson USA</td>
<td>663 M</td>
<td>18-65+</td>
<td>Every or most nights</td>
<td>15.3 M 8.2 F</td>
</tr>
<tr>
<td>Ohayon et al, 1997</td>
<td>UK</td>
<td>2078 M</td>
<td>15-100</td>
<td>Regularly</td>
<td>47.7 M 33.6 F</td>
</tr>
<tr>
<td>Marin et al, 1997</td>
<td>Zaragoza Spain</td>
<td>597 M</td>
<td>18-86</td>
<td>Usually or always</td>
<td>63.6 M 36.3 F</td>
</tr>
<tr>
<td>Neven et al, 1998</td>
<td>Krimpen Netherlands</td>
<td>1402 M</td>
<td>M ≥35  F ≥50</td>
<td>3 or more nights a week</td>
<td>38.7 M 20.1 F</td>
</tr>
<tr>
<td>Lindberg et al, 1998c</td>
<td>Uppsala Sweden</td>
<td>2668 M</td>
<td>40-79</td>
<td>Often or very often</td>
<td>20.4 M</td>
</tr>
<tr>
<td>Zielinski et al, 1999</td>
<td>Warsaw Poland</td>
<td>578 M</td>
<td>38-67</td>
<td>Often or always</td>
<td>48 M 27 F</td>
</tr>
<tr>
<td>Larsson et al, 2001</td>
<td>Norrbotten Sweden</td>
<td>2349 M</td>
<td>20-69</td>
<td>Snoring as a problem</td>
<td>14.6 M 6.7 F</td>
</tr>
</tbody>
</table>
snoring (Pickett et al, 1989; Popovic & White, 1998), while others have failed to demonstrate this (Cistulli et al, 1994). A protective effect of hormone therapy may be a result of an increased muscular tone in the upper airways (Keefe et al, 1999). As in men older than 60 years, older women have less problem with snoring (Honsberg et al, 1995; Lindberg et al, 1998c). The reason for this decline in the oldest subjects is unclear. It is perhaps more common for older subjects to live alone, lacking someone to register their snoring, but it is probably not exclusively due to reporting bias (Young et al, 1996; Lindberg et al, 2000).

In concordance with our results, several authors have found gender differences in snoring with a man to woman ratio of approximately 2:1 (Redline et al, 1994; Young et al, 1996). Most authors report also that women with OSAS are heavier than men with the same severity of AHI (Guilleminault et al, 1988; Ambrogetti et al, 1991; Young, 1993). In our general population study we have no information of BMI, but in our bronchitic cohort study, BMI was associated with both snoring as a problem and concern about witnessed apnea, to a similar degree in both men and women. The intensity of the snoring sound is higher in men than in women (Wilson et al, 1999). That can possibly explain part of the difference in experiencing snoring as a problem.

Relatives' concern about witnessed sleep apnea

Reported relatives' concern about witnessed sleep apnea followed the same age-pattern as snoring, but the gender difference was greater. Others have reported similar results (Enright et al, 1996).

Daytime sleepiness

Lindberg et al (1998b) found increased mortality in subjects below 60 years old reporting both snoring and EDS. EDS and other daytime symptoms are important consequences of snoring and OSA. In our study we asked if the subjects were rested after a full nights sleep, and if they had a tendency to nod off in breaks in activity in the daytime. Not rested in the morning was four times more common than the tendency to nod off during the daytime. Men reported nod off significantly more often than women but women with
snoring as a problem reported both daytime symptoms, especially not rested, more often than snoring men did. Women with snoring seem to have more daytime sleepiness, which is in accordance with reports of others (Chervin, 2000).

Early in the study of OSA, investigations were done on subjects referred for sleep studies, and one major purpose was to find instruments to reduce the amount of patients for sleep recordings. It was sometimes hard to associate daytime sleepiness with OSA, but the studied cohorts were already highly selected (Dealberto et al., 1994). In recent studies EDS has been clearly associated with both snoring and OSA (Johns, 1993; Young et al., 1993; Zielinski et al., 1999; Gottlieb et al., 2000). Snoring without OSA was also associated with EDS (Stradling & Crosby, 1991; Guilleminault et al., 1993). This strengthens the opinion that the main cause of EDS in OSA and UARS is sleep fragmentation (Martin et al., 1997; Berry & Gleeson, 1997), but oxygen desaturation may contribute to EDS in OSA (Cheshire et al., 1992; Punjabi et al., 1999). Further, treatment with CPAP reverse much of the daytime symptomatology (Guilleminault et al., 1993; Pillar & Lavie, 1998).

Relatives’ concern about witnessed apnea and snoring as a problem were independently associated with daytime sleepiness in our study. Chronic productive cough, rhinitis, and current smoking were also independently associated with EDS, while age, gender, and asthma were not. It is easy to understand that obstructive respiratory diseases can give sleep disruption, and there are studies that have found daytime sleepiness in respiratory diseases obvious due to sleep disturbances. In subjects with chronic bronchitis, both EDS and insomnia are reported (Kauffmann et al., 1989; Klink et al., 1994). Asthma is also associated with daytime sleepiness in many studies (Klink & Quan, 1987; Janson et al., 1990; Fitzpatrick et al., 1993; Janson et al., 1996), but not in all. Tucson Epidemiologic Study of Obstructive Airways Disease found a significant relationship between EDS with coexistent chronic bronchitis, concomitant asthma and chronic bronchitis, and emphysema, but not with asthma as a solitary diagnosis (Klink & Quan, 1987).

Most subjects have probably experienced some sort of sleep disturbance during acute rhinitis. Our results confirmed other studies reporting increased daytime sleepiness in subjects with rhinitis (Janson et al., 1996; Young et al., 1997c; Craig et al., 1998).
RESPIRATORY DISEASES

Bronchitis

There are a few reports, including from the Tucson epidemiologic study of obstructive airways disease, that have found snoring to be more common in subjects with chronic bronchitis, especially in combination with smoking (Bloom et al., 1988; Klink et al., 1994; Honsberg et al., 1995). In our study we found that subjects with bronchitic symptoms reported snoring as a problem, concern about witnessed sleep apnea, and also daytime sleepiness twice as often as non-bronchitics. The relationship remained even after adjustments for age, gender and smoking habits. The figures were almost the same in both the bronchitic cohort study and in the general population study, which strengthens the relationship between sleep apnea and bronchitis. In the bronchitic cohort study (Paper I), snoring as a problem tended to be more commonly reported in subjects with recurrent wheeze and chronic productive cough compared with only sputum production and long-standing cough. Chronic productive cough is close to chronic bronchitis as defined by Ciba Guest Symposium (CIBA Guest Symposium, 1959; Lundbäck, 1993), while especially long-standing cough is a more non-specific bronchitic symptom and often a mark for non-chronic respiratory disorder. Recurrent wheeze is a sign of obstructive pulmonary disorder, but can be associated with asthma as well as with chronic bronchitis (Lundbäck et al., 1991; Fitzpatrick et al., 1993) and even more directly with smoking (Pallasaho et al., 1999; Kotaniemi et al., 2001; Lindström et al., 2001).

In the validation study (Paper III), we found a high prevalence of OSA in subjects with bronchitic symptoms. The figures are minimum figures, since there are probably subjects with OSA that did not report snoring in the previous part of the study, and hence were not invited to sleep studies. The subjects without respiratory complaints and with snoring as a problem were few, but there is no indication that problem with snoring would predict OSA in a different way in healthy subjects than it would for subject with bronchitic symptoms. Based on this assumption the prevalence of OSAS (defined as AHI≥10 with concomitant daytime sleepiness symptoms) was twice as high in bronchitic than in non-bronchitic subjects. The prevalence of OSAS in bronchitic subjects was 5.4% and calculated to be 2.3% in subjects without respiratory disease. As a comparison, Young et al (1993) found a
corresponding prevalence in the Wisconsin study of 2.3% in men and 1.1% in women in a working population, which is close to the prevalence in healthy subjects in our study. This indicates that not only snoring, but also the sleep apnea syndrome, is common in subjects with bronchitic symptoms.

It is suggested that the inflammation in bronchitis affects not only the bronchi, but also the pharynx with swelling of the soft tissue hence predisposing to SDB by narrowing of the upper airways. Sputum production may contribute to increased upper airway resistance. Another possibility is gastroesophageal reflux (GER) as a link between bronchitis and OSA. Chronic persistent cough was in one study a consequence of GER in 5% of the cases (Kardos & Gebhardt, 1996). Reports indicate that OSA is one cause of GER (Keller & Breitenbucher, 1990; Kerr et al, 1992b; Ing et al, 2000). Others have found no temporal relation between reflux and obstructive sleep apnea event, and state that gastro-esophageal reflux and obstructive sleep apnea are two separate disorders, which both have a high prevalence in obese patients (Graf et al, 1995; Penzel et al, 1999). On the other hand, the negative intrathoracic pressure during sleep apnea might predispose to reflux in susceptible subjects, and by aspiration lead to chronic bronchitis. Reducing the negative intrathoracic pressure with CPAP effectively reduces nocturnal GER even in patients without OSA (Kerr et al, 1993; Ing et al, 2000).

COPD and lung function

The overlap syndrome, which is OSA with concomitant COPD, is known to cause a more severe disease (Krieger et al, 1989; Kessler et al, 1996) with high morbidity and mortality (Fletcher et al, 1991; Chaouat et al, 1999). It is also thought that chronic bronchitis is a predictor of, and precedes COPD (Lundbäck et al, 1994; Vestbo et al, 1996). COPD is a common disease (Bakke et al, 1991), and the question arises if COPD is more common in subjects with OSA. It is generally considered that the overlap syndrome is just coincidental, but there are a few studies that have found decreased FEV₁ in OSA patients (Zerah-Lancner et al, 1997; Appelberg et al, 2000). In our large bronchitic cohort, FEV₁ percent predicted was, as expected, decreased in subjects with bronchitic symptoms. Although bronchitic subjects reported more snoring we found that neither snoring as a problem or OSA were associated with a decrease in FEV₁. This strongly suggests that COPD and OSA, two common diseases, occur independent of each other.
Asthma

Nocturnal asthma is a common problem (Turner-Warwick, 1988), with sleep complaints (Janson et al, 1990) and symptoms of daytime dysfunction (Fitzpatrick et al, 1991). There are reports that snoring and OSA can provoke asthma (Chan et al, 1988), and CPAP treatment of asthmatics with concomitant OSA eliminates not only sleep apnea, but also nocturnal asthma attacks (Chan et al, 1988; Guilleminault et al, 1988b). In our study we found that subjects with physician diagnosed asthma reported snoring as a problem and relatives’ concern about witnessed sleep apnea to a higher degree, and that asthma was independently associated with snoring and apneas after adjustment for age, sex, smoking habits, chronic productive cough, and rhinitis. Increased bronchial hyperreactivity was found in a small sample of patients with OSA, and the hyperreactivity decreased after 2-3 months on CPAP therapy (Lin & Lin, 1995). Janson et al (1996) found, in a multicenter study, higher prevalence of both snoring and apneas in asthmatic subjects. However, they did not find any association between BHR and snoring or apneas. In another study, high prevalence of snoring among asthmatics was reported, especially among young wheezers (Fitzpatrick et al, 1993). Others have not found association between snoring and asthma (Norton & Dunn, 1985). Co-existing rhinitis has been proposed to be responsible for higher prevalence of snoring among asthmatics, but in our study asthma was independently associated with snoring and apneas after adjustment for rhinitis.

Rhinitis

There are many reports about the association between rhinitis and snoring or OSA. Physiologically, an increased nasal resistance will result in increased negative pressure in the airways with increased risk for upper airway collapse (Olsen et al, 1981; Cole & Haight, 1984; Gleson et al, 1986). However, the relation is complex. In our study, a history of rhinitis was independently associated with both snoring as a problem and relatives’ concern about witnessed sleep apnea. Most studies have found an association between rhinitis and snoring or apneas (McNicholas et al, 1982; McColley et al, 1997), but without strong association between magnitude of nasal obstruction and severity of SDB (Olsen & Kern, 1990; Young et al, 1997c).
Others have found no association between snoring and rhinitis (Bloom et al., 1988; Miljeteig et al., 1993).

SMOKING HABITS

Smoking has decreased in Sweden during the last decade, but still, according to our study, in the general population in Norrbotten 1992, 32% of women and 29% of men were current smokers. Smoking habits is associated with snoring and OSA (Jenum & Sjol, 1992; Delasnerie-Laupretre et al., 1993). In our study current smoking, but not ex-smoking, was independently associated with both snoring as a problem and witnessed sleep apnea. Interestingly, both smoking and bronchitic symptoms were independent of each other associated with snoring as a problem. Smoking has also been shown to have an exposure-effect relationship with snoring (Kauffmann et al., 1989; Wetter et al., 1994), and ex-smokers are at the level of never smokers within a few years (Bloom et al., 1988). This has led to the hypothesis that smoking acts by upper airway inflammation and edema (Bloom et al., 1988), but there are also other theories. Snoring may be a consequence of a decline in nicotine blood level throughout the night and perhaps the reverse, smoking as a consequence of snoring, to cope with daytime sleepiness (Wetter et al., 1994).

RECOGNITION IN HEALTH CARE

Two decades ago, snoring and OSA were regarded a predominantly male disorder. Today OSA is recognised as a disease that affects both men and women, though there still are gender differences in referral patterns to sleep laboratory. In a community sample males suffered from SDB 2-3 times more often than women, but in sleep lab sample the man:woman ratio was 8-10:1 (Redline et al., 1994; Young et al., 1997b). Women were thus underserved in a ratio of 3:1 (Young et al., 1996). During the first decade that sleep studies have been performed in Norrbotten less than 20% of all subjects with reported snoring as a problem or relatives’ concern about witnessed sleep apnea were referred to sleep lab. If all subjects with snoring as a problem or relatives’ concern about witnessed apnea had sought medical advice for their symptoms, then it would have comprised 13% of the adult population. The
difference in referral rate between men and women in Norrbotten was less than previously reported from Wisconsin, USA. After adjustment for difference in reported symptoms in the community, the man:woman ratio in Norrbotten was 1.25:1. Thus women are still, but to a lesser degree than in Wisconsin, underserved in Norrbotten. The reason for this gender difference in referral rates is unclear. Do women have different symptoms of SDB (Ambrogetti et al, 1991), do they complaint less, or do health care providers disregard symptoms of OSA in women?
CONCLUSIONS

- Snoring as a problem, relatives’ concern about witnessed apnea, and symptoms of daytime sleepiness were more common in subjects with bronchitic symptoms.

- Snoring as a problem, relatives’ concern about witnessed apnea, and symptoms of daytime sleepiness were not associated with lung function impairment.

- Snoring as a problem reflected OSA and OSAS to a high degree.

- The prevalence of OSA was higher in subjects with bronchitic symptoms compared with subjects without respiratory complaints.

- In a general population, snoring as a problem and relatives’ concern about witnessed apnea were associated with chronic bronchitis, asthma, and rhinitis. Daytime sleepiness was associated with chronic bronchitis and rhinitis but not with asthma.

- In subjects aged 20-69 years, the prevalence for snoring as a problem, relatives’ concern about witnessed apnea, not being rested after a full nights sleep, and tendency to nod off in the daytime were in men 14.6%, 11.0%, 26.0%, and 6.9% respectively. Corresponding figures in women were 6.7%, 2.4%, 24.7%, and 5.3%.

- Snoring, apneas and nod off were significantly more common in men. The prevalence of snoring and apneas increased with age but decreased in older men and women. Other independent risk factors for snoring and apnea were current smoking and socio-economic groups including higher educated and self-employed, while for daytime sleepiness they were apnea, snoring, and current smoking. Women with snoring as a problem expressed daytime sleepiness to a higher degree than men did.

- The result indicates that in the last decade less than 20% of all subjects in the population with snoring as a problem or relatives’ concern about witnessed apnea were referred to sleep lab. Women
were underserved with a man:woman ratio of 1.25. The amount of sleep apnea recording available in Norrbotten seems to be underdimensioned compared with the need in the population.
The need for investigations of snoring and sleep apnea is high since about 18% of men and 7% of women experience snoring to be a problem or have relatives that are concerned about witnessed sleep apnea. Snoring and sleep have serious consequences, such as daytime sleepiness including dysfunction in skill and performance, mood alteration, impaired social functioning and reduced quality of life. Cardio-vascular diseases are more common and the combination COPD and OSA, the overlap syndrome has a bad outcome. This study has shown that subjects with bronchitis have more problem with snoring and OSAS, and as bronchitics are at risk of developing COPD, it is important not to forget OSA and in extension the overlap syndrome in those with snoring and other symptoms giving suspicion of SDB. This study is the first study reporting smoking and bronchitis as independent risk factors for snoring. Smoking cessation should therefore be regarded as a part in the treatment of snoring and OSA. It is further important to listen also to women’s complaints of SDB, since women, though they have more daytime sleepiness, are underserved at sleep apnea investigations.
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78


81


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