Increased mortality among sleepy snorers: a prospective population based study

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Abstract

Background—The long term health consequences of snoring and sleep apnoea syndrome are still uncertain. This study was conducted to assess the mortality risk associated with snoring and excessive daytime sleepiness (EDS), the two main symptoms of sleep apnoea syndrome, in men.

Methods—In 1984 a sample of 3100 men aged 30–69 responded to a postal questionnaire including questions about snoring, EDS, and the prevalence of various diseases (response rate 77%). Mortality data for the period 1985–1995 were collected for the complete sample.

Results—During the 10 year follow up period 213 men died, 88 of cardiovascular diseases. Compared with subjects with no snoring or EDS in 1984, men with isolated snoring or EDS displayed no significantly increased mortality. The combination of snoring and EDS was associated with a significant increase in mortality. However, the relative rates decreased with increasing age, and in men aged 60 and above no effect on mortality was found. Men below the age of 60 with both snoring and EDS had an age adjusted total death rate which was 2.7 times higher than men with no snoring or EDS (95% CI 1.6 to 4.5). The corresponding age adjusted hazard ratio for cardiovascular mortality was 2.9 (95% CI 1.3 to 6.7) for subjects with both snoring and EDS. Further adjustment for body mass index and reported hypertension, cardiac disease, and diabetes reduced the relative mortality risk associated with the combination of snoring and EDS to 2.2 (95% CI 1.3 to 3.8) and the relative risk of cardiovascular mortality to 2.0 (95% CI 0.8 to 4.7).

Conclusion—Snoring without EDS does not appear to carry an increased risk of mortality. The combination of snoring and EDS appears to be associated with an increased mortality rate, but the effects seems to be age dependent. The increased mortality is partly explained by an association between “snoring and EDS” and cardiovascular disease.

Methods

POPULATION

A random sample of 4021 men aged 30–69 was drawn from the population registry of the city of Uppsala, Sweden in 1984. The population
### Table 1 Age stratified and age adjusted total number of deaths/person years and mortality rates per 1000 person years among responders and non-responders

<table>
<thead>
<tr>
<th>Age</th>
<th>No snoring, no EDS (n=1352)</th>
<th>Snoring without EDS (n=1051)</th>
<th>EDS without snoring (n=346)</th>
<th>Snoring and EDS (n=23)</th>
<th>Total (n=3100)</th>
<th>Non-responders (n=921)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–39</td>
<td>4/583 (0.7%)</td>
<td>5/2971 (1.7%)</td>
<td>1/1860 (0.5%)</td>
<td>6/1286 (4.7%)</td>
<td>16/11949 (1.3%)</td>
<td>6/3558 (1.7%)</td>
</tr>
<tr>
<td>40–49</td>
<td>3/3160 (0.9%)</td>
<td>9/3021 (3.0%)</td>
<td>4/858 (4.7%)</td>
<td>4/837 (4.8%)</td>
<td>20/7876 (2.5%)</td>
<td>8/2516 (3.2%)</td>
</tr>
<tr>
<td>50–59</td>
<td>17/1902 (8.9%)</td>
<td>15/2241 (6.7%)</td>
<td>2/344 (5.8%)</td>
<td>11/703 (15.6%)</td>
<td>45/5190 (8.7%)</td>
<td>38/1481 (25.7%)</td>
</tr>
<tr>
<td>60–69</td>
<td>57/2192 (26.0%)</td>
<td>52/1895 (27.4%)</td>
<td>8/330 (24.2%)</td>
<td>15/520 (28.8%)</td>
<td>132/4907 (26.9%)</td>
<td>48/1173 (40.9%)</td>
</tr>
</tbody>
</table>

95% confidence intervals (CI) are presented for age-adjusted mortality rates.

### sample has been described in detail elsewhere.11 12 A postal questionnaire was sent to the subjects in the sample in December 1984. After two reminders, acceptably completed questionnaires were returned by 3100 participants (77.1%). Another 101 subjects responded but had omitted either the question on snoring or the one on EDS and were therefore regarded as non-responders in this case.

### QUESTIONNAIRE

The 24 questions used in the 1984 questionnaire included questions about snoring and sleep disturbances, daytime sleepiness, and somatic diseases.11 In addition, height and weight were asked for and body mass index was calculated. In the question about snoring the subjects were asked to state the frequency of their loud and disturbing snoring using a five point scale.12 The five response alternatives were never, rarely, sometimes, often, or very often. Those subjects who answered “never” or “rarely” were regarded as non-snorers, while subjects who reported loud and disturbing snoring “sometimes”, “often”, or “very often” were regarded as snorers. The responses to the question about daytime sleepiness were also given on a five point scale.11 The subjects were asked to state how many problems they experienced from daytime sleepiness. Possible responses were “no problems”, “small”, “moderate”, “severe”, and “very severe” problems. In the subsequent statistical evaluation, EDS was defined as the experience of daytime sleepiness as a moderate to very severe problem. On the basis of these criteria, symptoms at baseline were categorised into four groups: (1) no snoring and no EDS; (2) snoring but no EDS; (3) EDS but no snoring; (4) both snoring and EDS.

### VALIDATION OF THE QUESTION ABOUT EDS

As the question used here to measure EDS has not previously been validated, we compared it with the Epworth Sleepiness Scale (ESS) which has been shown to correlate significantly with sleep latency measured during multiple sleep latency tests.13 In an ongoing study, 189 men from the present study population have simultaneously answered the EDS question used here and the ESS questionnaire. Of the 141 men with scores of 1–2 for the EDS question, the mean ESS score was 5.9 (3.5) which is close to the ESS scores of 5.9 (2.2) described for healthy controls. The 48 men with scores of 3–5 for the EDS question had a mean ESS score of 8.9 (4.1), which is slightly lower than the mean score of 9.5 (3.3) described for patients with mild OSAS.13

The participants were asked to indicate whether they had hypertension, cardiac disease, or diabetes. In addition, three general questions were included about regular medical examinations, previous hospital care, and medication. The subjects were classified as having hypertension if they reported attending regular medical check ups for hypertension and/or answered “yes” to the question: “Do you have high blood pressure?” Diabetes was defined as answering “yes” to the question: “Do you have diabetes?” All the subjects who had been admitted to hospital or attended regular check ups due to diabetes were included in this group. Subjects were regarded as suffering from heart disease if they answered “yes” to the question: “Do you have cardiac disease?” or reported attending regular medical check ups due to angina pectoris or previous myocardial infarction, or had been in hospital as a result of any of these diagnoses.

### MORTALITY DATA

Mortality data for the 10 year period 1985–1994 were collected for the complete sample. Death certificates were obtained from the National Cause of Death Register in Sweden for all subjects who had died within the country. During the 10 year period 36 of the 3100 responders had emigrated to other countries. Of those who had moved abroad, three were reported as dead with a known date of death, but no information on the cause of death was obtained. Seven of the men who had moved abroad were located in a follow up survey in December 1994. Of the remaining 26 subjects who emigrated, the date of emigration was obtained for 19 and they were censored from that date. For the remaining seven men no date of emigration was obtained and they were censored from 1 January 1985.
and >28 kg/m²) in these calculations. When analysing the determinants of cardiovascular death, subjects who died of other causes were treated as censored observations. The results are presented as adjusted hazard ratios with 95% confidence limits.

### Results

Of the 3100 men who responded to the questionnaire in 1984, 1051 subjects (33.9%) were snorers without EDS according to the criteria mentioned above. EDS without snoring was reported by 346 (11.2%), while 351 (11.3%) suffered from both snoring and EDS.

Among the responders there were 213 deaths during the 10 year follow up period (mortality rate 7.1%). Death certificates were available for 208, based on necropsies in 102 (49.0%) cases. The main cause of death was cardiovascular in 88 cases (42.3%), cancer in 87 (41.8%), suicide in five (2.4%), accidents in five (2.4%), and other causes in 23 cases (13.5%). Age specific and age adjusted mortality rates by symptom groups at baseline are presented in table 1.

When calculating the associations between snoring, EDS and mortality, the group with no snoring or EDS was used as the reference group. In a Cox proportional hazards model snorers with no EDS and subjects with EDS but no snoring displayed no significant increase in the relative rates (RR) of mortality after adjustments for age (table 2). In contrast, men with both snoring and EDS displayed a significant increase in overall mortality. However, the relative rates of mortality among men with both “snoring and EDS” decreased with age and, in the oldest age group, the RR was only 1.1 (fig 1). When analysing the age group 30–59 years separately, men with both snoring and EDS had an age adjusted total death rate which was 2.7 times higher than men with no snoring or EDS (95% CI 1.6 to 4.5). The corresponding age adjusted relative ratio for cardiovascular mortality was 2.9 (95% CI 1.3 to 6.7) for subjects with both snoring and EDS. In men aged 60 and above no effect on mortality was found (table 2). When an interaction variable “(snoring and EDS) × (age 60–69 years)” was added to the Cox analysis, the adjusted hazard ratios for the interaction variable were significantly below 1.0 (OR 0.4 (95% CI 0.2 to 0.9) and 0.2 (0.05–0.7) for overall mortality and cardiovascular mortality respectively). The differences between the younger and older age groups when it came to the influence of “snoring and EDS” mortality was thereby significant. In the following calculations this interaction variable was included as soon as adjustments for age were made.

When compared with men with no snoring or EDS, men with snoring but no EDS were older while men with EDS but no snoring were younger (table 3). A significantly higher mean BMI as well as a prevalence of BMI of >28 was found in snorers, regardless of whether they had EDS or not. In a univariate analysis reported hypertension was somewhat more
common among snorers without EDS, while diabetes was associated with EDS without snoring. Subjects with the combination of snoring and EDS had a significantly higher prevalence of reported hypertension, diabetes and heart disease in 1984.

To see whether the mortality risk produced by snoring and EDS in men below the age of 60 was mediated through or caused by other factors, a set of multivariate life table analyses were performed. After adjustments for age, BMI, hypertension, heart disease, and diabetes in a Cox proportional hazards model, the RR of overall mortality among men with both snoring and EDS was reduced to 2.2 (95% CI 1.3 to 3.8) but it was still significantly higher (table 4).

When compared with the non-snoring men without EDS, men in the younger age group with both “snoring and EDS” ran an increased risk of cardiovascular death with an age adjusted RR of 2.9 (95% CI 1.3 to 6.7). The RR was only slightly reduced when adjustments were made for BMI and hypertension in 1984. However, when heart disease and diabetes at baseline were added to the model as potential confounders, the RR of “snoring and EDS” was reduced to 2.0 and this was no longer significant (table 4). In the Cox analyses isolated snoring or EDS had no significant influence on overall mortality or cardiovascular mortality, regardless of the number of independent variables added. Furthermore, the interaction variable “(snoring and EDS) × (age 60–69)” was significantly below 1.0 in all the calculations.

As the influence on mortality of snoring and EDS was only significant in men below 60 years of age, the causes of death among men aged 30–59 were studied more carefully. Of the 2546 subjects in this age group, 837 (32.9%) were snorers without EDS, 312 (12.2%) had EDS without snoring, and 293 (11.5%) suffered from both snoring and EDS. During the 10 year follow up 90 of the subjects died. Of the 293 men aged 30–59 with both snoring and EDS, 21 died during the 10 year period. In this group nine (3.1%) died from cardiovascular causes compared with 10 (0.9%) of the 1104 men in this age group with no snoring and no EDS (p<0.01). The corresponding rates for death due to cancer were six (2.0%) versus nine (0.8%) (NS) and three (1.0%) versus one (0.09%) (p<0.01) for suicide. Of the remaining three men aged 30–59 with snoring and EDS who died, one died of a subdural hematoma, one of pancreatitis, and the cause of death was unknown for one man who died abroad.

As no significant associations were found between isolated snoring or EDS and mortality, the men with the combination of snoring and EDS were compared with all the remaining men in a survival analysis. As shown in fig 2, among men aged 30–59 the cumulative survival rate was significantly lower for subjects with “snoring and EDS”.

Alcohol dependence as an underlying or contributory cause of death was mentioned in nine of the death certificates. Two belonged to the group with both snoring and EDS aged 30–59 (9.5%). In the corresponding age group alcohol dependence was mentioned for six of the 69 men without “snoring and EDS” (8.7%).

In the whole population a total of 92 men reported in 1984 that they had one or more of the diseases for which adjustments were made here (hypertension, cardiac disease and/or diabetes), as well as “snoring and EDS”. Adding the interaction variable “(any disease 1984) × (snoring and EDS)” to the Cox analyses did not significantly influence the results; there were still no associations between isolated snoring or EDS and mortality, while the age adjusted hazard ratios for “snoring and EDS” were 2.4 (95% CI 1.4 to 4.4) and 2.9 (95% CI 1.2 to 7.1) for overall mortality and cardiovascular mortality, respectively.

**Figure 2** Survival analysis of men aged 30–59 years in 1984 who reported snoring and excessive daytime sleepiness (EDS) or without both snoring and EDS at baseline.
Increased mortality among sleepy snorers

NON-RESPONDERS
Of the 921 men who did not respond to the questionnaire in 1984 100 died during the 10 year period. A necropsy was performed in 58 cases (58.0%). Forty seven of the deaths (47.0%) were cardiovascular and 21 (21.0%) were due to cancer. Four of the non-responders (0.4%) committed suicide and, in the case of one, it was not known whether death was due to suicide or accident. The mean age at death was 63.4 (9.0) years (95% CI 61.5 to 65.3) for the non-responders and 64.4 (9.7) years (95% CI 63.1 to 65.7) for the responders (NS).

The mortality rates for non-responders are presented in table 1. Compared with the responders, the non-responders had a higher overall mortality with an age adjusted RR of 1.8 (95% CI 1.4 to 2.3). Moreover, the RR of cardiovascular death increased to 2.1 (95% CI 1.5 to 3.0) after adjustment for age. The corresponding RR of death due to cancer was 0.9 (95% CI 0.6 to 1.5). When analysing the 30–59 age group the corresponding relative risks were: overall mortality 2.2 (95% CI 1.6 to 3.1), cardiovascular death 2.5 (95% CI 1.4 to 4.4), and death from cancer 1.5 (95% CI 0.8 to 2.9).

Discussion
In this population based study no association was found between snoring without daytime sleepiness and mortality. However, among men who reported both snoring and EDS at baseline, the total mortality as well as the cardiovascular mortality during the 10 year follow up period increased significantly compared with other men, but the difference decreased with age.

Excessive daytime sleepiness and heavy snoring are the typical complaints of patients with OSAS and patients with upper airway resistance syndrome (UARS). In 1985 a prevalence survey of OSAS was performed in this study population, including whole-night polysomnography. Of the men with “snoring and EDS” in the present study, 57 were included in that investigation, 15 of whom (26.3%) were found to suffer from OSAS. The number of men who suffered from UARS is unknown because at that time we were unaware of that disorder. Even though the inclusion criteria for the polysomnographic study in 1985 were based on a somewhat different definition of “snoring and EDS” we can assume that a substantial proportion of the snoring and sleepy men had indeed been suffering from respiratory disorders during sleep (OSAS or UARS).

In previous surveys designed to study mortality in patients with OSAS increased mortality was found by some researchers but not by others. Of the four studies in which younger OSAS patients were also included, an increased mortality rate was reported in three, but in the retrospective study conducted by Gonzalez-Rothi et al which included 91 patients with OSAS (24 of whom were untreated), no increase in mortality was found. In that study, however, the mean follow up time was less than three years and the reference group consisted of 35 non-apnoeic patients with symptoms suggestive of OSAS.

No influence on mortality by snoring and EDS was found in this study of men above 60 years of age. This is in accordance with previous studies of patients with OSAS. In a prospective study by Lavie et al the authors found that the apnoea index was a predictor of excess mortality in the fourth and fifth decade but not in elderly men. When investigating elderly populations, no association was found between apnoea-hypopnoea scores and mortality in two prospective studies while in another study a significant association was seen only in women. It therefore seems reasonable to conclude that, at least in males, the health consequences of sleep disordered breathing seem to decrease with age.

In our population of men below 60 years of age with snoring and EDS, both the overall mortality and cardiovascular mortality was increased. When investigating OSAS patients, Partinen et al found an increase in vascular mortality in the conservatively treated group when compared with patients treated with tracheostomy. In addition, high prevalences of OSAS are described in patients with ischaemic heart disease and stroke. The exact mechanisms which explain why OSAS gives rise to cardiovascular disease are unclear, but conceivable explanations are the physiological responses to repetitive desaturations associated with acidosis and changes in intrathoracic pressure, as well as the increase in sympathetic activity seen in patients with OSAS.

In a recent review of research on the health consequences of OSAS, the authors concluded that the evidence for a causal association is weak and raised the question of whether sleep apnoea is a separate disease entity or a marker or a symptom of obesity and ageing. From the results obtained in this study we can assume that, within the group with “snoring and EDS” the prevalence of OSAS is high, but it is also mixed up with subjects not suffering from this disease. Despite this suggestion, the adjusted hazard ratio for mortality for the men in the younger age group with “snoring and EDS” was only slightly reduced when age and BMI were taken into account. Furthermore, when the subjects with both snoring and EDS are regarded as a group with a high prevalence of OSAS, it could be argued that the high prevalence of hypertension and cardiac disease is a consequence of the disease and should not be regarded as a confounder. If this is true, the adjustments in table 4 lead to an underestimation of the association between “snoring and EDS” and mortality. Adding the interaction “(any disease 1984) × (snoring and EDS)” did not significantly change the results, thereby indicating that the results obtained here relating to the influence of snoring and EDS on mortality are valid for subjects both with and without pre-existing disease.

It is noteworthy that, among men aged 30–59, the number of suicides was three
among the 293 men with both snoring and EDS and only two among the 2253 without these symptoms. This result may be a consequence of depression which is often seen in patients with OSAS. We found that daytime somnolence was a significant predictor of the incidence of stroke and coronary heart disease during a 10 year follow up. In the cited article, however, the occurrence of snoring was not taken into account. When analysing our results in a similar manner—that is, comparing men with EDS with all the remaining men without considering snoring—reported EDS in 1984 was a significant predictor of overall mortality, as well as cardiovascular death, with age adjusted RRs of 1.9 (95% CI 1.2 to 3.0) and 2.3 (95% CI 1.1 to 4.9), respectively. Here too, an interaction variable “EDS × age 60–69” was significantly negative.

One disadvantage of this study is that no information on smoking status was collected at baseline. In a prospective study of mortality in relation to smoking habits the death rate ratio over a period of 20 years (comparing continuing cigarette smokers with life-long non-smokers) was approximately threefold at age 45–64. It is well known that smoking is associated with snoring as well as obstructive sleep apnoea syndrome and smoking must be looked upon as a potential confounder in this context. By using the methods proposed by Axelson the magnitude of such an influence could be assessed. In our study, among the responders in 1984 89.7% of the survivors responded to a follow up questionnaire in 1994 including questions about current and past smoking habits. Of the survivors who responded in 1994, 46% of the men aged 30–59 with both snoring and EDS in 1984 were smokers that year compared with 33% of the rest. If we make the extreme assumptions that the prevalence of smoking was 70% among subjects with snoring and EDS who died, and that the RR of dying for smokers increased threefold during 10 years, the RR with adjustment for smoking could be calculated. For subjects with snoring and EDS the RR for overall mortality with adjustment for age and smoking would then be 2.2 (95% CI 1.4 to 3.6).

The mortality rate was significantly higher among the non-responders. In previous Swedish surveys higher mortality has also been reported among subjects who do not take part in population studies. We can therefore expect our responders to be more healthy than the non-responders. About 11% of the responders suffered from both snoring and EDS. The prevalence of snoring and EDS among non-responders might influence the results. To assess the magnitude of the potential bias we assumed that every fifth (20%) non-responder at random had snoring and EDS. For the complete sample with both snoring and EDS the age adjusted RR of all-cause mortality would then be 2.7 (95% CI 1.6 to 4.5) and 2.9 (1.3 to 6.7) in the case of cardiovascular mortality. If, on the other hand, the prevalence of snoring and EDS is only 5% among the non-responders, the corresponding RRs are 2.0 (95% CI 1.3 to 3.1) and 2.1 (1.01 to 4.3), respectively. This means that the effect of selective non-participation on the results is small and does not affect the conclusions. We conclude that, in a random sample of middle aged men from the population, snoring without EDS does not appear to influence the mortality rate.

The combination of snoring and EDS appears to be associated with an increased mortality rate but the effect seems to be age dependent. The increased mortality is explained at least in part by an association between “snoring and EDS” and cardiovascular disease. We suggest that, in epidemiological studies of snoring, the occurrence of EDS should be taken into account. Furthermore, in surveys in which the health consequences of snoring, OSAS and UARS are investigated, the role of age should be carefully considered.

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