



## Prevalence and risk factors of excessive daytime sleepiness in insomnia sufferers: A study with 1311 individuals



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### ABSTRACT

**Background:** Several studies have investigated the prevalence and risk factors of excessive daytime sleepiness in the general population. However, few studies have investigated these in the particular subpopulation of insomnia sufferers. Thus, the aim of this study was to examine the prevalence and risk factors of excessive daytime sleepiness in a large sample of insomnia sufferers.

**Methods:** Data from 1311 insomnia sufferers with age  $\geq 18$  years and recruited from the research database of the sleep laboratory of the Erasme Hospital were analysed. A score  $> 10$  on the Epworth scale was used as the cut-off score for excessive daytime sleepiness. Logistic regression analyses were conducted to examine clinical and demographic risk factors of excessive daytime sleepiness in insomnia sufferers.

**Results:** The prevalence of excessive daytime sleepiness in our sample was 45.61%. Multivariate logistic regression analysis revealed that non-use of Z-drugs, non-use of Trazodone alone or in combination, body mass index  $\geq 25$  &  $< 30$  kg/m<sup>2</sup>, body mass index  $\geq 30$  kg/m<sup>2</sup>, age  $\geq 18$  &  $< 40$  years, age  $\geq 40$  &  $< 65$  years, Beck depression inventory score  $\geq 5$  &  $< 16$ , Beck depression inventory score  $\geq 16$ , apnea-hypopnea index  $\geq 15$ /h, and use of selective serotonin reuptake inhibitors were significant risk factors of excessive daytime sleepiness in the subpopulation of insomnia sufferers.

**Conclusion:** Excessive daytime sleepiness is a common complaint for individuals with insomnia. In this subpopulation, most of the risk factors for excessive daytime sleepiness are reversible, which justifies better management of this complaint to avoid its negative consequences.

### 1. Introduction

Excessive daytime sleepiness (EDS) is a common complaint in the general population where it is present in 18% to 27% of individuals [1–3]. In addition, it is associated with a higher risk of car accidents, occupational accidents and cardiovascular mortality, as well as a diminished quality of life [4–7]. EDS is therefore an important public health issue requiring adequate screening and management to avoid such deleterious consequences.

Complaints related to daytime functioning, including EDS, are also very common in insomnia [8,9]. Indeed, EDS is present in 16% to 28.1% of insomnia sufferers [10,11]. In addition, insomnia is a risk factor for EDS [12]. Despite the existence of this particular relationship, EDS is currently under-studied and under-diagnosed in insomnia sufferers as it is often confused with symptoms indicative of insomnia, such as fatigue [13]. Therefore, the establishment of appropriate

management for the specific subpopulation of insomnia sufferers is necessary to better diagnose and prevent the consequences of EDS.

In the general population, many risk factors for EDS have been identified, including obesity, complaints of insomnia, depression, obstructive sleep apnea syndrome (OSA), male gender, younger age, alcohol consumption, and smoking [14–20]. However, most of these risk factors have not been validated in the particular subpopulation of insomnia sufferers.

Moreover, some treatments frequently used in the management of insomnia, such as benzodiazepines, Z-drugs (such as Zolpidem, Zopiclone and Zaleplon), and antidepressants may have the occurrence of sedation and EDS as side effects [21–26]. Essentially, these different treatments could induce or even aggravate EDS in insomnia sufferers. Thus, it is important to determine which treatments are actually associated with a greater risk of EDS in the subpopulation of insomnia sufferers.

**Abbreviations:** AHI, Apnea-Hypopnea Index; BDI, Beck Depression Inventory; BMI, Body Mass Index; DSM IV-TR, Diagnostic and Statistical Manual of Mental Disorders fourth edition - Text Revision; EDS, Excessive Daytime Sleepiness; ESS, Epworth scale; ISI, Insomnia Severity Index; MAOI, Monoamine oxidase inhibitors; OSA, Obstructive Sleep Apnea Syndrome; REM, rapid eye movement sleep; SSRI, Selective Serotonin Reuptake Inhibitors; SNRI, Serotonin-norepinephrine reuptake inhibitors; TCA, Tricyclic antidepressants

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Our first objective was to investigate the actual prevalence of EDS in this subpopulation, and our second was to identify their specific risk factors for EDS. To achieve these goals, we recruited a large sample of insomnia sufferers that we divided into a control group without EDS and a patient group with EDS. The aim of this approach is to allow health professionals who treat patients with insomnia to understand the importance of this problem in this subpopulation and to better identify those at risk of EDS, which ultimately will facilitate a diagnosis currently made difficult by the existence of an overlap between symptoms of insomnia and EDS.

## 2. Materials and methods

### 2.1. Population

The sample was comprised of 1311 insomnia sufferers recruited from the database of the sleep laboratory of Erasme Hospital. The database contains data for 3511 individuals who completed sleep laboratory monitoring in the years 2002–2014. In our study, we only recruited insomnia sufferers because our objective was to focus on the subpopulation where the existence of an overlap between the symptoms of insomnia and EDS makes the diagnosis of this complaint more difficult.

These insomnia sufferers were referred to the sleep laboratory by physicians specializing in sleep medicine after an ambulatory consultation during which a preliminary assessment of complaints related to sleep, ongoing treatments, somatic and psychiatric comorbidities was carried out systematically, making it possible to conduct a first diagnostic hypothesis. Following this first assessment, a sleep laboratory was offered to all insomnia sufferers to exclude the presence of other sleep pathology and obtain an objective evaluation of their sleep. Moreover, the data obtained during this ambulatory consultation are systematically checked when the subjects are admitted to the sleep laboratory.

The inclusion criteria were age  $\geq 18$  years, the presence of diagnostic criteria A (complaint of difficulty initiating [defined as sleep latency  $\geq 30$  min at least  $3 \times$ /week] or maintaining sleep [defined as 3 or more nocturnal awakenings or a long nighttime awakening (30 min or more) or early morning awakening (30 min or more before the usual time) at least  $3 \times$ /week], or non-restorative sleep, for at least 1 month) and diagnostic criteria B (the sleep disturbance or associated daytime fatigue causes clinically significant distress or impairment in social, occupational, or other important areas of functioning) of insomnia from the Diagnostic and Statistical Manual of Mental Disorders fourth edition - Text Revision (DSM IV-TR) [27].

The exclusion criteria included the presence of a major psychiatric disorder (psychotic disorder), uncontrolled heavy somatic disease, chronic pulmonary disease, inflammatory or infectious disease, history of cranial trauma, history of central nervous system injury that could involve respiratory centres in the brain, history of craniofacial or thoracic cavity malformations, pregnancy, OSA already diagnosed or course of treatment before sleep laboratory, predominantly central apnea syndrome, narcolepsy or primary hypersomnia, parasomnia, and presence or history of substance abuse.

## 3. Methods

### 3.1. Medical and psychiatric evaluation of participants

Upon admission to the sleep laboratory of Erasme Hospital, all subjects had their medical records reviewed and a complete somatic check-up performed, including a blood test, electrocardiogram, a daytime electroencephalogram, urinalysis and a chest X-ray (only for those over the age of 45). These steps allowed for a systematic diagnosis of potential somatic pathologies present in people admitted to our unit.

Patients also benefited on the day of admission from an

appointment with a unit psychiatrist who potentially assigned psychiatric diagnoses per the DSM IV-TR criteria [27].

On admission, patients completed a series of self-questionnaires to assess the severity of their subjective complaints of depression, insomnia, and excessive daytime sleepiness as follows:

- The presence of depressive symptoms was investigated using the Beck Depression Inventory (BDI reduced to 13 items). This scale consists of 13 items that can be scored from 1 to 3. The final score can vary from 0 to 39. A final score of 0–4 indicates an absence of depression, 5–7 a slight depression, 8–15 a moderate depression, and  $> 16$  severe depression [28].
- Daytime sleepiness was investigated using the Epworth scale (ESS). This scale consists of eight questions that can be scored from 0 to 3 and assesses sleepiness during different daytime situations. The final score varies from 0 to 24. A final score  $> 10$  indicates EDS [29].
- The presence of insomnia symptoms was investigated using the Insomnia Severity Index (ISI). This index consists of seven questions that can be scored from 0 to 4. The final score can vary from 0 to 28. A score of 0–7 indicates a lack of insomnia, 8–14 subclinical insomnia, 15–21 moderate insomnia, and 22–28 severe insomnia [30].

To avoid missing values, only individuals who responded fully to these questionnaires were included in our study.

### 3.2. Sleep evaluation and study

A psychiatrist of the unit conducted a sleep-specific medical record systematic review on the day of admission to complete an assessment of complaints related to sleep including sleeping habits, symptoms of sleep apnea (snoring and self-reported apneas), symptoms of restless legs syndrome, and nocturnal movements (e.g., periodic movements of the limbs). Insomnia was diagnosed after this appointment if the diagnostic criteria A and B for insomnia according to DSM IV-TR [27] were met.

Participants stayed in a sleep laboratory for two nights, including a first night of habituation and a second night of polysomnography from which the data were collected for analysis. The patients went to bed between 22:00–24:00 and got up between 6:00–8:00, following their usual schedule. During bedtime hours, the subjects were recumbent and the lights were turned off. Daytime naps were not permitted.

The polysomnographic recordings from our unit met the guidelines of the American Academy of Sleep Medicine (AASM) [31]. The applied polysomnography-montage was as follows: two electro-oculogram channels, three electroencephalogram channels (Fz-Ax, Cz-Ax, and Oz-Ax, where Ax was a A1A2 mastoid reference), one submental electromyogram channel, electrocardiogram, thermistors to detect the oronasal airflow; finger pulse-oximetry, a microphone to record breathing sounds and snoring, piezoelectric sensors, strain gauges to measure thoracic and abdominal breathing, and leg movement electrodes. Polysomnographic recordings were visually scored by specialized technicians using AASM criteria [32] (inter-judge agreement score of 85%).

Apneas were scored if the decrease in airflow was  $\geq 90\%$  for at least 10 s, whereas hypopneas were scored if the decrease in airflow was  $\geq 30\%$  for at least 10 s with a decrease in oxygen saturation of 3% or followed by a micro-arousal [33]. Apnea-hypopnea index (AHI) corresponds to the total number of apneas and hypopneas divided by period of sleep in hours. OSA was considered mild when AHI was  $\geq 5/h$  and  $< 15/h$  and moderate to severe when AHI was  $\geq 15/h$  [34].

### 3.3. Statistical analyses

Statistical analyses were performed using Stata 14. The normal distribution of the data was verified using histograms, boxplots, and quantile-quantile plots, and the equality of variances was checked using

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