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ORIGINAL ARTICLE

Health, social, and economic consequences of rapid eye movement sleep behavior disorder: a controlled national study evaluating societal effects

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Abstract

Study Objectives: Parkinson's disease (PD) causes significant socioeconomic burdens. One of the strongest predictors of PD is rapid eye movement (REM) sleep behavior disorder (RBD; when there is no known other cause of RBD, referred to as idiopathic RBD [iRBD]), but there is no information about its factual welfare burden. We estimated the direct and indirect total costs of iRBD in a national sample of patients, based on a national register-based cohort study with matched controls.

Methods: Using records from the Danish National Patient Registry, patient's diagnosis with RBD from 2006 to 2016 were identified. We excluded patients with a prior diagnosis of narcolepsy, PD, and other neurodegenerative diseases. We identified and compared randomly chosen controls matched for age, gender, geographic area, and civil status. Direct costs included frequencies of primary and secondary sector contacts and procedures, and medication. Indirect costs included the effect on labor supply. Social-transfer payments were included to illustrate the effect on national accounts.

Results: A total of 246 iRBD patients and 982 matched controls were registered. iRBD patients had significantly higher rates of health-related contacts and of medication use, and higher socioeconomic costs than controls. The total additional direct net healthcare costs after the diagnosis (general practitioner services, hospital services, and medication) and indirect costs (loss of labor market income) was €13,088 for patients compared with controls. Patients already exhibited a negative social- and health-related status several years before the first diagnosis.

Conclusions: Diagnoses of iRBD have major socioeconomic consequences for patients, their partners, and society.

Statement of Significance

This is the first large scale study of the economic consequences of rapid eye movement sleep behavior disorder. We report the entire socioeconomic cost including primary, secondary care, lost income, and increases in welfare transfer. Other studies have focused on small populations in specialized centers, in this study we include the entire national population.

Key words: REM sleep behavior disorder; economic; epidemiology

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Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia of REM sleep closely linked to Parkinson's disease (PD), and the use of RBD as a biomarker of the development of PD is currently attracting considerable interest [1]. RBD is often seen in patients with PD, but may also be apparent during the decade before PD develops (known as idiopathic RBD, in patients where there is no other known cause of RBD). This makes it potentially valuable for the prompt detection of early developmental stages of alpha-synucleinopathies, which may be exploited to provide protective treatment involving neuroprotective drugs [2, 3]. RBD may also be associated with hypocretin-deficient narcolepsy [4, 5], structural lesions in the brain [6], and other causes [7], this subtype of RBD is classified as secondary RBD. The prevalence of iRBD is uncertain, but estimated to be 1% or less among adult or elderly population [8, 9]. There are currently no data regarding the societal burden of iRBD. Here we aimed to estimate the total societal welfare cost of iRBD from a national sample of patients diagnosed with iRBD.

Methods

In Denmark, it is possible to calculate health sector costs and productivity losses related to diseases because information from public and private hospitals, general practice, privately practicing specialists, medication, social transfers, labor market income, and employment for all Danes is registered in central databases. All patient contacts with the hospital system, and the primary diagnosis, are recorded in the Danish National Patient Registry (NPR) at the time of contact. The NPR is a time-based national database that includes data from all inpatient and outpatient contacts, meaning that the data that we can extract are representative of everyone in Denmark who has received a diagnosis of iRBD in public and private hospitals. Since data are available for the entire observation period, we can trace patients retrospectively and prospectively, relative to the time of their iRBD diagnosis. Furthermore, all contacts in the primary sector (general and specialist practices) and medication use are recorded in the databases of the National Health Security and the Danish Medicine Agency, respectively. We have used this dataset and setup to analyze a variety of diseases [10–14].

The prevalence of iRBD in the population is significantly underestimated, as the population in general, and health professionals in particular, are largely unaware of the disease. The economic consequences of iRBD for patients and their partners were estimated by determining the yearly cost of illness per patient diagnosed with the ICD-10 code for RBD (DG4752); these codes are given after patient evaluation in each hospital, often at a specialized sleep center. The diagnostic code includes cases of REM sleep without atonia as well as RBD, as there is currently no international code distinguishing these conditions.

The RBD diagnosis is present in the data from 2006, so the population consists of patients diagnosed in the period 2006–2016. Since the analysis requires an after-period of 3 years, we included only the 451 RBD patients with an index date in the period 2006–2013.

We selected the patients on the condition of not having the following ICD10 diagnosis in the period from 1994 to the index date G474 (narcolepsy), G471 (hypersomnia), G209 (PD), G318E (Lewy body dementia), G230–G239 (degenerative disorders of the basal ganglia: multiple system atrophy and progressive supranuclear palsy), and G30 (Alzheimer's disease).

By excluding the 205 cases and 10 controls from the data with co-morbid neurodegeneration or narcolepsy, we are left with 246 iRBD patients with an index in the period 2006–2013. A total of 166 were male and 80 female, and their average age was 52.1 (*SD* 17.6) years. This is a very small number when considering that the total Danish population with an age of 67 or above is slightly more than one million (in 2020). We would expect 10,000 iRBD patients just from the elderly population. iRBD patients were compared with those of an individual matched control group based on gender, age, civil status, and municipality. From the total Danish population, we selected 982 controls (without RBD, narcolepsy, or neurodegeneration), giving a ratio of cases to controls of approximately 1:4. Matches were obtained in 99.8% of cases. The estimated health cost was then divided into annual direct and indirect healthcare costs. Direct costs, including hospitalization, costs of outpatient visits, and uses of medication, were calculated using diagnosis-related group weights, and specific outpatient tariffs. These cost estimates were all based on data from the Danish Ministry of Health. The use and costs of drugs were calculated from data provided by the National Danish Medicine Agency, and consisted of the retail price of each drug (including dispensing costs) multiplied by the number of transactions. The frequencies and costs of consultations with general practitioners and other specialists were based on data from National Health Security. The indirect costs (foregone earnings), which are those related to reduced labor supply, are based on figures from Danish Income Statistics. Social-transfer payments, which are primarily publicly funded in Denmark, were also included. These include subsistence allowances, pensions, social security, social assistance, publicly funded personal support for education, and others. Cost-of-illness studies measure the economic burden resulting from disease and illness across a defined population, and consider direct and indirect costs. As patients leave the national data registers at the time of death, disappearance, or emigration, the indirect cost estimate comprises only the production loss related to disease-related work disability. It is important to distinguish health-related costs from monetary transfer payments such as disability and welfare payments. These payments transfer purchasing power to the recipients from general taxpayers, but do not represent net increases in the use of resources, for which reason they are not included in the total cost estimate. From the NPR, we identified all people who received a first diagnosis of iRBD between 2006 and 2016. Then, using data from the Civil Registration System and the Statistics Denmark database (which include information about social factors, marital and cohabiting status, incomes, pensions, etc.), we randomly selected citizens who had the same age and sex as those with RBD. Social compensation was taken into account by selecting control subjects who resided in the same area of the country in which the patients lived, and who had the same civil status. Patients and matched control subjects were followed from the year of diagnosis until 2016. Thus, people with an iRBD diagnosis at the beginning of the period contributed follow-up data over 10 years; those experiencing an iRBD diagnosis at the end of the period provided pre-diagnosis data, and all those in between provided varying amounts of pre- and post-diagnosis data. If a patient or control was not present in the CPR register on January 1st each year, then the corresponding control or person with iRBD control was not included in the dataset for that year. People with iRBD who are absent from the CPR register are typically deceased, in prison, or have emigrated to another country.

Costs were measured on a yearly basis and adjusted to 2009 prices using the general price index. All costs were measured in DKK and converted to Euros using the exchange rate on June 30, 2011 (1 Euro = 7.45 DKK).

The study was approved by the Danish Data Protection Agency. Data were handled in a manner that did not reveal the identity of anyone with iRBD or of any control subjects, so neither individual nor ethical approval was required. Statistical analysis was done with SAS 9.1.3 (SAS Inc., Cary, NC). Statistical significance of the cost estimates was assessed by nonparametric bootstrap *t*-test.

Results

Health care costs

The total healthcare costs for patients with iRBD were a mean of €7,290, compared with €3,344 for controls in the year of diagnosis.

RBD patients had a greater home care cost, lower income, and increased public transfer cost, resulting in an increased total cost to society of €13,088 in the year of diagnosis. The complete expenses are shown in Table 1. Supplementary Table S1 with median and interquartile range (IQR Q3–Q1) available online.

We analyzed the total health costs 3 years before and 2 years after the diagnosis (Figure 1).

iRBD patients incur a greater health care cost, even during the 3 years before the diagnosis, indicating that iRBD is not an isolated phenomenon but part of a larger disease complex.

Table 1. Healthcare costs for patients with iRBD and Controls in €.

	RBD	Control	p^*
Number of persons (*N*)	246	982	
Somatic			
Outpatient services	1,568	1,116	0.016
Inpatient admissions	3,643	1,389	<0.001
Prescription drugs	876	364	<0.001
Primary health sector	727	381	<0.001
Somatic health costs total	**6,813**	**3,250**	<0.001
Psychiatric outpatient services	177	22	<0.001
Psychiatric inpatient admissions	300	72	0.005
Health costs total (including psychiatric costs)	**7,290**	**3,344**	<0.001
Home care			
Home care—care	392	416	1.000
Home care—practical help	63	57	1.000
Home care total	**455**	**473**	1.000
Earned income (wage, self-employed)	**21,139**	**27,796**	<0.001
Public transfer			
Unemployment benefit (A-kasse)	444	510	1.000
Unemployment benefit	1,576	497	<0.001
Age pension	4,594	4,686	1.000
Early retirement	808	685	0.999
Disability pension	2,285	1,327	<0.001
Sick pay (public-funded)	820	260	<0.001
Housing benefits	413	405	1.000
Childs benefits	176	244	0.368
Public transfer income total	**11,116**	**8,615**	<0.001
Direct health costs	7,290	3,344	
Home care costs	455	473	
Indirect costs, foregone earnings	6,657		
Sum of direct and indirect costs	**14,403**	**3,816**	
Net costs	10,586		
Social transfer payments	11,116	8,615	
Net costs, including transfers	**13,088**		

Significant differences are indicated in bold.
*Probability associated with *t*-test. Home care cost data were only available from 2009. Psychiatric costs were available from 2007

Discussion

This is the first study to evaluate the total welfare burden in a national sample of iRBD patients compared with controls. We found that iRBD was associated with significantly elevated direct and indirect costs before and after the disease diagnosis.

The total increase in healthcare expenditure and socioeconomic cost is comparable to that previously found in PD patients measured in the same population using the same registers [10]. The lost income is more dominant in the iRBD population than in the PD population because the iRBD patients are younger than the PD patients.

Previous studies have found significant welfare consequences of PDs and other alpha-synucleinopathies, including a negative effect on quality of life, increased health care use, social impact, such as reduced work capabilities, and increased home care use [15, 16]. Recent studies have indicated a significant impact on quality of life and highlighted a variety of health-related consequences of non-motor symptoms in PD [17–19]. Here we show that one of these manifestations, iRBD, causes a significant welfare burden. The largest meta-analysis [20], of 46 studies, comprising 3,262 patients with a PSG-confirmed diagnosis of RBD, found a range of other pre-Parkinson's symptoms that are consistent with the idea of iRBD patients having a greater comorbid burden, which, in this study, is reflected in the increased welfare burden.

iRBD should be regarded as a serious neurological disease because it has important consequences for the patient arising from its association with PD. The disease has substantial economic consequences for patients and society.

More research is needed in large populations of iRBD patients. The prevalence of the iRBD diagnosis in different countries will influence the economic cost per patient. In some countries, the diagnosis may only be made rarely, in the most severe cases.

If RBD is to be used as a diagnostic marker for developing neuroprotective strategies, its association with other diagnostic markers at the epidemiological scale must be ascertained. It is important to establish iRBD as a marker for neurodegeneration in order to develop neuroprotective medication given that the iRBD cohort is a highly suitable group in which to test new medication. Determining the total cost and consequences of iRBD may help in this regard.

Limitations and Strengths of the Findings

This is a register study so diagnoses are not validated, and no information on the use of diagnostic criteria, diagnostic procedures, or the qualifications of doctors applying the diagnoses is available. Only hospitals can enter diagnostic codes in the central registers. The diagnostic certainty is lower than in controlled cohort studies, although this it is known to be very high in the Danish registers [21]. The strength of this study is that it includes all patients in the country. The national registers are complete and cover the entire population in the areas

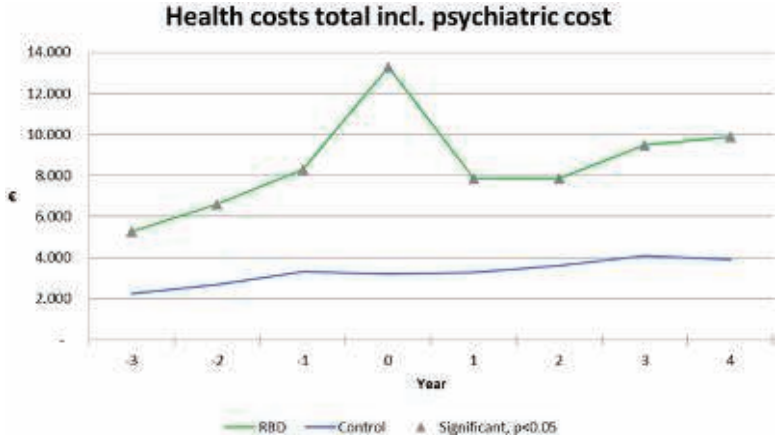

Figure 1. Cohort with index date in the period 2001–2007. Analysis of health care costs in the period 2006–2016. Total costs total including psychiatric costs prior to and after diagnosis. The cost for each time-point is significantly higher for iRBD patients than for controls. The adjusted *p*-values are from the bootstrapped *t*-test for case versus controls.

of medical diagnosis, medical expenses, prescriptions of medication, income, taxes, education, social benefits, place of residence, etc., all of which are linked to personal social security numbers. It is also a strength that these data are available at the national level, making them better suited for evaluating the total cost nationally than are small studies of selected patients from specialist centers. We excluded patients with a diagnosis of narcolepsy/hypersomnia or neurodegenerative disease. Patients with these diseases who are not registered as having them, but are registered as having RBD, appear in this dataset.

This study is based on a vast dataset that includes all socioeconomic data, comorbidities, and medication. This is too large a subject for a single study and further papers will be based on this dataset.

Conclusions

We found that iRBD patients incur a significant socioeconomic burden compared with healthy controls. The total home care cost, lower income, and higher public transfer cost results in a greater total cost to society of €13,088 per patient. This increase is slightly higher than that seen in PD [10]. The reason for this may be that iRBD patients are diagnosed at specialist centers with expensive polysomnography, while some PD patients are diagnosed by a GP or a private practice neurologist with no expensive diagnostic procedures. It may also be the case that iRBD patients who develop PD in their PD state have more early autonomic symptoms, reflecting a larger burden of neurodegeneration. These autonomic symptoms would result in more visits to hospitals with a wide range of symptoms. iRBD patients are younger and have a greater loss of economic income than do PD patients, who tend to be older.

Our experience with other sleep centers has revealed to us that most hospital systems use only the first three, rather than all the digits of the ICD-10 system for coding diseases, causing RBD and other parasomnias to be registered under the same code. We urge all centers that diagnose sleep disorders to start using the full ICD-10 coding system, which recognizes the subdiagnosis of parasomnias such as non-REM (DG475A) and RBD (DG4752). A validation of this study could be possible in the other Nordic countries as they have similar central registers and public hospitals, but most other countries do not have the complete information in central registers needed for this type of study.

Supplementary Material

Supplementary material is available at *SLEEP* online.

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