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Prevalence of sleep disturbances in people with epilepsy and the impact on quality of life: a survey in secondary care

Therese Gutter[a,*], Petra M.C. Callenbach[b], Oebele F. Brouwer[b], Al W. de Weerd[a]

[a] Department of Clinical Neurophysiology and Sleep Centre SEIN Zwolle, the Netherlands
[b] Department of Neurology, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands

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ABSTRACT

Purpose: Studies in adults with epilepsy, mainly in specialized epilepsy clinics, have shown that sleep disturbances were twice as prevalent in people with epilepsy as in healthy controls. Our aim was to determine the prevalence of sleep disturbances in people with epilepsy treated in district hospitals, as well as the impact of it on Quality of Life.

Method: Adults with epilepsy, attending outpatient clinics in three district hospitals were invited to participate. Those who accepted (N = 122) provided their own controls matched for age and sex. Both groups completed four questionnaires (Groningen Sleep Quality Scale (GSQ), Medical Outcomes Study-Sleep scale (MOSS), Sleep Diagnosis List (SDL) and Epworth Sleepiness Scale) to measure their sleep over different periods and the 36-Item Short Form Health Survey (SF-36) to measure Quality of Life (QoL). The prevalence of sleep disturbances and scores on QoL were compared between both groups.

Results: Sleep quality, measured by the SDL, was in the pathological range 50% more often in the epilepsy group than in controls. This was confirmed by the $MOSS_{INDEX}$ and GSQ. People with epilepsy experienced excessive daytime sleepiness more often than controls.

The lowest scores on nearly all domains of the SF-36 were seen in people with epilepsy and associated sleep disturbances.

Conclusion: We confirmed the higher prevalence of sleep disturbances in people with epilepsy compared to controls as previously reported from specialized settings. The (co-morbid) sleep disturbances result in lower QoL scores, in both people with epilepsy and in controls, but more in people with epilepsy.

1. Introduction

Subjective sleep disturbances are more often seen in people with epilepsy (PWE) than in healthy controls. Questionnaire-based studies in specialized epilepsy clinics suggest that more than a third of adults with refractory epilepsy have a sleep disturbance, twice as often as in controls [1,2]. In children with epilepsy, the prevalence of sleep disturbances is even higher, being ten times that of classmates of the same age without epilepsy [3]. In the general community, the prevalence of obstructive sleep apnea syndrome (OSAS) is up to 13% [4,5], but the prevalence is up to 63% in PWE [6,7]. Insomnia occurs in 20–52 % of PWE [8–10].

The relationship between sleep and epilepsy is bidirectional. Sleep disturbances with lack of sleep can result in increased seizure frequency. Conversely, nocturnal seizures, side-effects of anti-epileptic drugs (AEDs) and psychological or psychiatric problems related to epilepsy, may influence sleep quality [8,11,12]. Sleep problems have a negative influence on quality of life, especially in PWE in whom lower scores can be expected than in those without epilepsy [1,12,13].

Most reports of sleep disturbances in PWE are from people with refractory seizures attending epilepsy specialized clinics or tertiary care. Prevalence of sleep disturbances in people treated in secondary care district hospitals is unknown. These people usually have less severe epilepsy with lower seizure frequency and use lower doses of AEDs, because according to national guidelines they would have been referred to tertiary care in case of not getting seizure-free within two years or if three AEDs have failed. With this study, we tried to estimate the prevalence of subjective sleep disturbances and their influence on quality of life in PWE attending district hospitals compared to people without epilepsy.

* Coressponding author at: Stichting Epilepsie Instellingen Nederland (SEIN), Dr. Denekampweg 208025 BV ZWOLLE, the Netherlands.
E-mail address: tgutter@sein.nl (T. Gutter).

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2. Methods

This questionnaire-based, cross-sectional study was conducted in the departments of Neurology of three district hospitals in the north-eastern part of the Netherlands. One neurologist in each hospital searched the hospital databases for individuals with a definitive diagnosis of epilepsy and asked them in writing to participate and to answer some questions about their current situation regarding seizure frequency, seizure type, use of AEDs and any visits to specialized epilepsy clinics. In case of questions about the study or the content of the information letter they could approach their own neurologist. Individuals who seemed to meet the inclusion criteria received the set of questionnaires.

2.1. Inclusion and exclusion criteria

People aged 18 years or older, with a definite diagnosis of epilepsy, were eligible. Epilepsy had to be active, with at least one seizure during the previous twelve months but if the seizure free period was over one year, daily use of AEDs to prevent relapse of seizures was required. Considering the fact that high seizure frequency and the occurrence of severe and/or long lasting seizures result in unstable situation that in itself affects their functioning and quality of life, only those with non-life threatening seizures with a frequency of less than once a week were included. Not more than two AEDs should be used daily, because it was assumed that people who used three or more AEDs for optimal seizure control, had a difficult to treat epilepsy and actually should be referred to a specialized epilepsy clinic. Each participant was asked to identify two people, not living together with the participant, of the same gender and age (± 2 years), to serve as controls. To be able to complete the questionnaires without help, participants had to be Dutch speaking with an educational attainment of elementary school at least. In case of questions or ambiguities regarding the questionnaires, the participants could contact the researchers by e-mail or telephone.

2.2. Questionnaires

All participants were asked to complete validated questionnaires measuring sleep quality, sleep problems and quality of life:

- The Groningen Sleep Quality Scale (GSQ) is a 14-item 'Yes' or 'No' questionnaire to estimate sleep quality during the previous night [14,15]. A score of less than 8 suggests disturbed sleep.
- The Medical Outcomes Study-Sleep (MOSS) scale is a 12-item questionnaire used to estimate sleep quality in the previous four weeks [16]. After recoding the original responses in a scale of 0–100, combinations of different items result in scores of probability of specific sleep problem domains: $MOSS_{SLEEP\ DISTURBANCE}$ (insomnia/sleep maintenance), $MOSS_{SNORING}$, $MOSS_{BREATHING\ DISORDER/HEADACHE}$, $MOSS_{SLEEP\ ADEQUACY}$, $MOSS_{DAYTIME\ SOMNOLENCE}$ and $MOSS_{DURATION\ OF\ SLEEP}$. Another parameter, the $MOSS_{SLEEP\ INDEX}$, the mean score of nine items, is an indicator of sleep quality; scores above 35 indicate sleep problems.
- The Sleep Diagnosis List (SDL) is the validated Dutch translation of the Sleep Diagnosis Questionnaire List [17,18]. It contains 75 questions about sleep over the past six months and covers six dimensions of sleep-related disturbances: insomnia, sleep apnea, narcolepsy, periodic leg movements, excessive daytime sleepiness and psychiatric sleep disorder. The questions are scored on a 5-point Likert scale, with 1 = never to 5 = very often or always. In each dimension a total mean score of 3 or more is indicative of the presence of that sleep disturbance.
- The Epworth Sleepiness Scale (ESS) is a questionnaire about how often a person dozes off during day-to-day activities [19,20]. For scores of 10 or higher the level of daytime sleepiness is considered pathological.
- The 36-Item Short Form Health Survey (version 2) (SF-36) is a Dutch translated and multi-purpose short-form health survey with 36 items, divided into eight health domains [21–23]. From these domains the psychometrically-based physical component summary (Physical Health) and the mental component summary (Mental Health) can be derived. The raw scores of each scale (mean of all items of each scale) are converted to T-scores, with a standardized mean score of 50 and standard deviation of 10. Higher scores reflect a better quality of life.

Characteristics of subjective sleep disturbances were explored using the GSQ, MOSS, SDL and the ESS. The ESS was used to investigate specifically sleepiness during the day.

The SDL was used as the primary test to indicate a sleep disturbance, endorsed by the results of the MOSS, ESS and GSQ.

Details of medical history, drug intake and educational level were recorded to complete demographic data.

2.3. Distribution of the questionnaires

Participants were sent three sets of questionnaires; one set to complete themselves and two extra sets to be completed by their controls.

2.4. Statistical analysis

Statistical analyses were performed with SPSS 24.0 (SPSS Inc., Chicago, IL). Comparison between PWE and controls was done using independent-sample t-tests or Mann-Whitney U tests, with Chi-square or Fisher Exact tests for categorical values. Spearman's rho was used to calculate the correlation between the questionnaires. Logistic regression was done to correct for the influence on sleep of age, gender, education, social status and co-morbidity. In the epilepsy group the influence of the treating hospital, use of AEDs, seizure type and seizures frequency on the prevalence of co-morbid sleep disturbances was analysed with multiple logistic regression. A p-value of < 0.05 was considered as significant.

The study was approved by the Medical Ethics Committee of the University Medical Centre of Groningen.

3. Results

Initially 139 patients agreed to participate in this study. Seventeen were excluded (low educational level, n = 1; not using AEDs and seizure free for more than one year, n = 6; not enough information, n = 10). The remaining 122 PWE identified 96 controls, but one had a history of seizures and was excluded. Additional male controls were needed and this was done with the help of colleagues. They asked relatives living in the immediate vicinity of the participating hospitals. Eventually 122 participants with epilepsy and 122 without epilepsy were included.

3.1. Demographic data

Demographic data are provided in Table 1. Education level was lower in PWE than in controls, but this did not result in differences between the groups in people in paid work. In addition to their epilepsy, more PWE mentioned co-morbidities than controls. Most prevalent were cardiovascular problems and pulmonary diseases.

Table 1
Demographic data of respondents, with and without epilepsy.

	People with Epilepsy N = 122	Controls N = 122	*p*-Value
Age Mdn (range)	56.2 (18.3-82.0)	60.3 (18.3-86.7)	0.451[a]
Sex Male n (%)	59 (48.4)	60 (49.2)	0.898[b]
BMI mean (SD) (range)	25.6 (4.0) (15-39)	25.6 (3.7) (18-42)	0.993[c]
Education			**0.003**[b]
- Elementary only n (%)	12 (9.8)	2 (1.6)	
- Elementary > < pre-univ n (%)	75 (61.5)	66 (54.1)	
- Pre-univ or higher n (%)	35 (28.7)	54 (44.3)	
Employed n (%)	68 (55.7)	80 (65.6)	0.088[b]
Comorbidity n (%)	59 (48.4)	43 (35.2)	**0.038**[b]
- Internal[d]	6	10	
- Neurologic	7	4	
- Pulmonal[d]	16	10	
- Cardiovascular[d]	35	26	
Age 1st seizure[e] Mdn (min-max)	43.0 (2-81)	–	
Duration of epilepsy[e] Mdn (range)	8.3 (0.2-66.2)	–	
Last seizure in months[f]		–	
< 1 month ago n (%)	29 (25.9)		
> 1 m < 3 mos ago n (%)	6 (5.4)		
> 3 mos < 1 yr ago n (%)	23 (20.5)		
> 1 year ago n (%)	54 (48.2)		
Number of AEDs		–	
- One AED n (%)	90 (73.8)		
- Two AEDs n (%)	25 (20.5)		
- Not specified n (%)	7 (5.7)		

SD: Standard Derivation.
pre-univ: pre-university (below high school level).
AED: Anti-epileptic drug.
BMI: Body Mass Index (kg/m^2).
[a] Mann-Whitney U test.
[b] Chi-squared test.
[c] T-test.
[d] twelve participants reported two chronic conditions.
[e] missing data in 23 people with epilepsy.
[f] missing data in 10 people with epilepsy.

3.2. Prevalence of sleep disturbances

PWE reported disturbed sleep more often than controls. The percentage of people with pathological scores in at least one of the SDL dimensions, was over sixty percent higher in the epilepsy group than in controls (Table 2B). The MOSS showed, as well as worse scores on the Sleep Index (Table 2A), also a higher percentage of people with sleep problems in the epilepsy group compared to the controls (Table 2B). The GSQ showed that the quality of sleep in the previous night was scored lower by PWE than by controls (Table 2A). The prevalence of a pathological GSQ score was almost 50% higher in PWE than in controls (Table 2B).

3.3. Details and characteristics of sleep disturbances

Excessive daytime sleepiness was more often scored pathologically by PWE than by controls.

The scores on $SDL_{EXCESSIVE\ DAYTIME\ SLEEPINESS}$ and the $MOSS_{SOMNOLENCE}$ were significantly higher in PWE than in controls (Table 2A), and a higher percentage of PWE scored pathologically on $SDL_{EXCESSIVE\ DAYTIME\ SLEEPINESS}$ (Table 2B). The scores on ESS did not confirm these findings despite the slightly higher percentage of pathological scores on this questionnaire by PWE compared with controls.

Although the median scores on $SDL_{INSOMNIA}$ did not differ, the number of PWE with pathological scores were more than twice as high as in controls, comparable with the findings in GSQ. The higher scores in the subscales $MOSS_{BREATHING\ DISORDER/HEADACHE}$, indicating a possible breathing problem during sleep, could not be confirmed by the scores on SDL_{APNEA}.

The consistency of subjective judgements of sleep was tested by the correlation between the different sleep questionnaires. $SDL_{SCORE\ PATHOLOGICAL}$, indicator if at least one of the SDL dimensions was scored pathologically, was correlated with the values measured with the other sleep scales. There was a moderate correlation between the general parameters; $SDL_{SCORE\ PATHOLOGICAL}$ and the Sleep Index scores of the MOSS [r_s: 0.459, $p < 0.001$]. The $SDL_{SCORE\ PATHOLOGICAL}$ correlated also moderately with the GSQ scores [r_s: -0.427, $p < 0.001$]. However, a strong correlation was found between the scores on $SDL_{EXCESSIVE\ DAYTIME\ SLEEPINESS}$ and the $MOSS_{DAYTIME\ SOMNOLENCE}$ [r_s: 0.825, $p < 0.001$] and moderate between $SDL_{EXCESSIVE\ DAYTIME\ SLEEPINESS}$ and the ESS [r_s: 0.641, $p < 0.001$], all three measuring excessive sleepiness during daytime.

The scales concerning obstructive sleep apnea correlated strongly [SDL_{APNEA} and $MOSS_{SNORING}$ [r_s: 0.755, $p < 0.001$]. Scales measuring insomnia and sleep maintenance correlated strongly between the domains $SDL_{INSOMNIA}$ and $MOSS_{SLEEP\ DISTURBANCE}$ [r_s: 0.816, $p < 0.001$] and moderately between $SDL_{INSOMNIA}$ and the sleep onset latency, first item of the MOSS [r_s: 0.588, $p < 0.001$], between $SDL_{INSOMNIA}$ and GSQ [r_s: -0.683 $p < 0.001$] and $SDL_{INSOMNIA}$ and $MOSS_{ADEQUACY}$ [r_s: -0.663, $p < 0.001$].

Table 2
Findings in sleep questionnaires in people with and without epilepsy.

	2A. Central Values of the scores			2B. Prevalence of pathological scores		
	People with epilepsy	**People without epilepsy**		**People with epilepsy**	**People without epilepsy**	
	Median (IQR_{25-75})	Median (IQR_{25-75})	*p*-value	Pathological % (n)	Pathological % (n)	*p*-value
Sleep Diagnosis List	N = 122	N = 122		N = 122	N = 122	
SDL score pathological				27.9% (34)	17.2% (21)	**0.046**[b]
Insomnia	1.9 (1.4-2.6)	1.9 (1.4-2.4)	0.325[a]	16.3% (20)	7.4% (9)	**0.030**[b]
Periodic leg movement syndrome	1.6 (1.1-2.3)	1.3 (1.0-2.0)	0.081[a]	9.0% (11)	8.2% (10)	0.819[b]
Excessive daytime sleepiness	1.7 (1.3-2.2)	1.5 (1.2-1.9)	**0.001**[a]	9.8% (12)	2.5% (3)	**0.016**[b]
Narcolepsy	1.1 (1.0-1.4)	1.0 (1.0-1.4)	0.052[a]	0.8% (1)	0	1.0[c]
Apnea	1.8 (1.4-2.4)	1.8 (1.4-2.1)	0.808[a]	5.7% (7)	4.1% (5)	0.554[b]
Psychiatric sleep disorder	1.9 (1.4-2.4)	1.6 (1.3-2.0)	**0.004**[a]	7.4% (9)	3.3% (4)	0.154[b]
Medical Outcomes Study-Sleep Scale	N = 120	N = 121		N = 120	N = 121	
Sleep Onset Latency > 30 minutes				21.7% (26)	18.2% (22)	0.498[b]
Sleep Disturbance	25.0 (10-41.3)	20.0 (10-35.6)	0.180[a]			
Snoring	40.0 (0-55)	40.0 (20-40)	0.283[a]			
Breathing disorder/headache	20.0 (0-40)	0 (0-20)	< **0.001**[a]			
Sleep Adequacy	65.0 (40-80)	80.0 (50-80)	0.063[a]			
Daytime Somnolence	33.3 (20-46.7)	20.0 (13.3-40)	< **0.001**[a]			
Sleep Quantity: hours sleep/night	7.0 (6-8)	7.0 (6-8)	0.328[a]			
< 7 and 8 hours sleep/night				38.8% (47)	30.6% (37)	0.162[b]
Sleep Index (9 items)	35.0 (28.9-41.4)	31.1 (24.7-38.3)	**0.005**[a]	50% (60)	36.4% (44)	**0.033**[b]
Groningen Sleep Questionnaire Scale	N = 121	N = 121		N = 121	N = 121	
	11 (7-13)	12 (8.5-13)	**0.026**[a]	36.4% (44)	24.8% (30)	0.051[b]
Epworth Sleepiness Scale	N = 117	N = 118		N = 117	N = 118	
	6.0 (4-10)	6.0 (3-8)	0.140[a]	26.5% (31)	16.9% (20)	0.076[b]

[a] Mann-Whitney U.
[b] Pearson Chi-square.
[c] Fisher's Exact.

3.4. Possible confounders

Age, gender, BMI, level of education or employment did not influence the prevalence of sleep disturbances in either group. The existence of co-morbidity other than epilepsy had influence on prevalence of a sleep disturbance. The odds of having a sleep problem increased two-fold [OR ($CI_{95\%}$): 2.147 (1.168–3.946] for all participants with a co-morbid illness. In the group of controls with a co-morbid illness the odd of having a sleep problem was 5.0 [OR ($CI_{95\%}$): 4.966 (1.819–13.588], while reported co-morbidity in people with epilepsy did not change these odds. Multivariate analysis of the influence of the different chronic illnesses on the prevalence showed that only a chronic cardiologic problem was significantly associated with the chance of having a sleep problem [OR ($CI_{95\%}$): 2.056 (1.005–4.205].This significant influence was found only in the controls [OR ($CI_{95\%}$): 4.000 (1.244–12.863], not in people with epilepsy [OR ($CI_{95\%}$): 1.202 (0.476–3.037]. Exclusion of people with cardiologic problems as possible confounder did not result in a change of the study result. The prevalence of sleep problems was higher in people with than without epilepsy. Comparison of the use of AEDs in the group of PWE showed that people without sleep disturbances significantly more often used one AED instead of two AEDs [84.1 vs. 15.9%] than those with a sleep disturbance [67.6% vs. 32.4%,$p = 0.045$]. No significant difference was observed in the seizure free period [Median (IQR): 22.8 (7.2–55.5) months and 14.4 (6.0–73.2) months respectively, $p = 0.645$].

3.5. Sleep disturbance and quality of life

PWE scored significantly lower on all subscales of the SF-36 than controls (Note: lower scores means lower QoL, Table 3A). The existence of a sleep disturbance, determined using the SDL scores, decreased the scores further (Table 3B). The same holds for the controls but these scores were still higher than in PWE (Table 3C).

The summary scores on Physical Health and Mental Health were also significantly lower in the epilepsy group than in controls (Table 3A, Fig. 1). The lowest scores were seen in PWE with a sleep disturbance on almost all SF-36 sub-scales (Table 3B). In this group the scores on the summary scales 'Physical Health' and 'Mental Health' were lower than those in the controls with sleep problems (Table 3C), but these differences were not significant [Physical Health: 58.7 (37.2–82.9) vs. 66.1 (49.6–84.6), $p = 0.299$; Mental Health: 59.5 (44.5–83.6) vs. 71.7 (53.5–84.8), $p = 0.400$].

4. Discussion

4.1. Prevalence of sleep disturbances

In this study in secondary care more PWE than controls reported sleep disturbances. This difference was less strong than shown in previous research in tertiary care [1,2]. One explanation for this difference could be the difference in severity of epilepsy. Formal comparison of the severity of the epilepsy between other studies is not possible, but it is known that in the tertiary care study of de Weerd et al [1] 40% of PWE used more than one AED, suggesting more refractory epilepsy [1]. This contrasts with our study in secondary care where only 20% were on polytherapy. Also, in the present study half of the PWE experienced their last seizure over a year ago. This implies more stable seizure control and may suggest that more complex epilepsy predisposes to more co-morbid sleep disturbances. Secondly, the age of the participants in the present study is ten years higher than in the previous survey [1]. Older age increases the risk of age-related sleep problems [24,25]. In older PWE complaints of insomnia or daytime sleepiness can

Table 3
Quality of life measured with SF-36 V2 in people with and without epilepsy and with and without a sleep disturbance. 3 A: Quality of life in both study groups, 3B: Quality of life in people with epilepsy with and without a sleep problem, 3C: Quality of life in Controls with and without a sleep problem.

	3 A: Total study population			3B. People with Epilepsy			3C. Controls		
	People with epilepsy N = 119	**People without epilepsy N = 120**	**M-W U test**	**People with epilepsy with sleep disturbance N = 34**	**People with epilepsy without sleep disturbance N = 85**	**M-W U test**	**Controls with sleep disturbanceN = 20**	**Controls without sleep disturbanceN = 100**	**M-W U test**
	Median (IQR_{25-75})	Median (IQR_{25-75})	***p*-value**	Median (IQR_{25-75})	Median (IQR_{25-75})	***p*-value**	Median (IQR_{25-75})	Median (IQR_{25-75})	***p*-value**
Physical Functioning	85 (65.0-95.0)	87.5 (85.0-100)	**< 0.001**	77.5 (40.0-95.0)	90.0 (75.0-97.5)	**0.026**	75.3 (51.3-88.8)	95.0 (90-100)	**< 0.001**
Social Functioning	87.5 (62.5-100)	100 (87.5-100)	**< 0.001**	75.0 (46.9-87.5)	87.5 (62.5-100)	**0.022**	87.5 (50.0-100)	100 (87.5-100)	**0.005**
Limitation due to Functional Health	68.8 (42.2-93.8)	93.8 (62.5-100)	**< 0.001**	50.0 (23.4-90.6)	75.0 (50.0-97.8)	**0.015**	53.1 (26.6-78.1)	93.8 (75.0-100)	**< 0.001**
Limitation due to Emotional Health	83.3 (58.3-100)	100 (75.0-100)	**< 0.001**	62.5 (25.0-100)	91.7 (66.7-100)	**0.005**	75.0 (50.0-100)	100 (83.3-100)	**0.012**
Emotional Well-Being	75.0 (65.0-90.0)	85.0 (75.0-90.0)	**0.008**	67.5 (50.0-81.3)	80.0 (70.0-90.0)	**0.002**	67.5 (60.0-80.0)	85.0 (75-90)	**< 0.001**
Energy/Fatigue	62.5 (43.8-75.0)	75.0 (62.-81.3)	**< 0.001**	50.0 (31.3-64.1)	68.8 (50.0-79.7)	**< 0.001**	50.0 (37.5-67.2)	75.0 (68.8-87.5)	**< 0.001**
Pain	77.6 (57.1-100)	94.9 (77.6-100)	**< 0.001**	67.3 (42.3-89.8)	79.6 (67.3-100)	**0.001**	72.4 (51.3-97.4)	100 (78.1-100)	**0.003**
General Health	60.0 (45-75)	75.0 (60-80)	**< 0.001**	47.5 (35.0-65.0)	65.0 (50-77.5)	**< 0.001**	67.5 (51.3-75.0)	75.0 (65-80)	**0.032**
Physical Health*	72.7 (54.1-86.3)	86.5 (74.1-93.4)	**< 0.001**	58.7 (37.2-82.9)	79.0 (61.4-86.8)	**0.002**	66.1 (49.6-84.6)	87.5 (79.6-93.8)	**< 0.001**
Mental Health*	77.8 (57.4-87.3)	86.3 (75.4-92.8)	**< 0.001**	59.5 (44.5-83.6)	80.0 (62.4-87.6)	**0.002**	71.7 (53.5-84.8)	88.6 (81.3-93.3)	**< 0.001**

M-W U test: Mann-Whitney U test.
* Summary of sub-scales of SF-36.

be the result of their age or can occur additionally to their epilepsy–related sleep problems, in the older controls they are new. This could partly explain the smaller difference in prevalence between PWE and controls in the current study compared to previous research.

Pathological scores on the SDL dimensions indicating insomnia, excessive daytime sleepiness and psychiatric sleep disorder were found much more often in PWE than in controls. For psychiatric sleep disorder however, the difference was not significant.

These findings were broadly in line with the higher central values and higher prevalence of pathological scores for the Medical Outcomes Study-Sleep Scale, $MOSS_{INDEX}$, and the lower scores for the Groningen Sleep Questionnaire Scale, GSQ. These trends are in accordance with previous findings [1,2,26–28]. The same holds for the Epworth Sleepiness Scale (ESS), the gold standard for sleepiness during daytime, even though the prevalence difference of almost 50% was not significantly different in our study [29,30].

Chronic health problems were mentioned by a third of controls. Especially cardiological problems were shown to have a strong influence on the chance of having a sleep problem. The apparently high prevalence of sleep disturbances in this group may be the consequence of the high percentage of this chronic comorbidity in this group.

4.2. Influence of sleep disturbances on Quality of Life of PWE

The existence of a sleep disturbance influenced QoL in both groups, PWE and controls, in all domains. It was most noticeable in the group with epilepsy. With this study in PWE in secondary care, it appears that having a sleep disturbance has a further negative impact on the quality of life, similar to findings in those in tertiary care [1]. Adequate diagnosis and careful treatment of these sleep problems, apart from the treatment of the epilepsy, is of clinical importance, mainly because of the strong interaction between the two diagnoses.

The low scores on ‘Physical Health’ and ‘Mental Health’ in controls with a sleep disturbance did not differ significantly from those in PWE with a sleep disturbance, suggesting that the existence of a sleep disturbance may strongly influence QoL.

4.3. Limitations

The number of people who agreed to participate was small. This is partly due to the study design where PWE attending secondary care were asked to participate in a study which was started and executed by a less familiar tertiary hospital. Also the way of distributing questionnaires and asking participants to complete the questionnaires at home, may have led to some bias. Still, despite the large range and standard deviations, we believe that our figures are reasonable.

Completing the questionnaires was done at home and not observed by one of the researchers. Therefore, clarification of uncertainties had to be done by e-mail or telephone. However, this was the same for both people with epilepsy and controls. Questionnaire studies in Sleep Medicine often provide prevalence figures higher than in studies where an extensive history and polysomnography are undertaken. The same holds for the exact sleep diagnosis. The differences found are, however, clear enough for the conclusion that sleep disorders occur more often in PWE and have a major effect on QoL in these people. The performed multiple comparisons may have provide lower *p*-value.

5. Conclusion

The prevalence of sleep problems is higher in PWE, not only in those with severe forms of epilepsy, but also in those with lower seizure frequency or seizure freedom as seen in secondary care.

Sleep problems worsen quality of life in people with and without epilepsy. Having a chronic disease, in particular epilepsy, increases the chance of developing an additional sleep disturbance which can result in further worsening of quality of life.

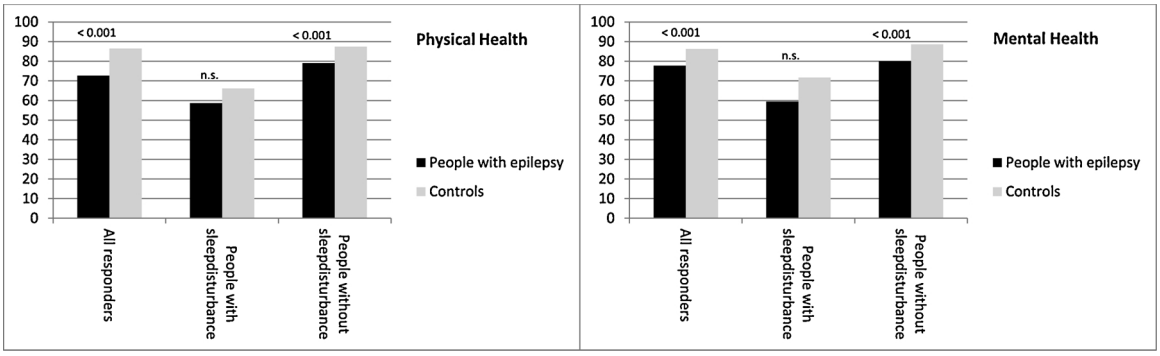

Fig. 1. Summary of the physical and mental health components of the SF-36 scale in PWE and controls, with and without sleep problems.

Conflicts of interest statement

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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References

[1] De Weerd A, De Haas S, Otte A, et al. Subjective sleep disturbance in patients with partial epilepsy: a questionnaire-based study on prevalence and impact on quality of life. Epilepsia 2004;45(11):1397–404.
[2] Ismayilova F, Demir AU, Tezer FI. Subjective sleep disturbance in epilepsy patients at an outpatient clinic: a questionnaire-based study on prevalence. Epilepsy Behav 2015;115:119–25.
[3] Gutter T, Brouwer OF, de Weerd AW. Subjective sleep disturbances in children with partial epilepsy and their effects on quality of life. Epilepsy Behav 2013;28:481–8.
[4] Peppard P, Young T, Barnet J, et al. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177(9):1006–14.
[5] Knuistingh Neven A, Middelkoop HAM, Kemp B, et al. The prevalence of clinically significant sleep apnoea syndrome in the Netherlands. Thorax 1998;53(8):638–42.
[6] Höllinger P, Khatami R, Gugger M, et al. Epilepsy and obstructive sleep apnea. Eur. Neurology 2006;55(2):74–9.
[7] Malow B, Weatherwax K, Chervin R, et al. Identification and treatment of obstructive sleep apnea in adults and children with epilepsy: a prospective pilot study. Sleep Med 2003;4:509–15.
[8] Khatami R, Zutter D, Siegel A, et al. Sleep-wake habits and disorders in a series of 100 adult epilepsy patients-A prospective study. Seizure 2006;15(5). 299-230.
[9] Vendrame M, Yang B, Jackson S, et al. Insomnia and epilepsy: a questionnaire-based study. J Clin Sleep Med 2013;9(2):141–6.
[10] Piperidou C, Karlovasitou A, Triantafyllou N, et al. Influence of sleep disturbance on quality of life of patients with epilepsy. Seizure 2008;17(7):588–94.
[11] Kwan P, Yu E, Leung H, Leon T, et al. Association of subjective anxiety, depression, and sleep disturbance with quality-of-life ratings in adults with epilepsy. Epilepsia 2009;50(5):1059–66.
[12] Jacoby A, Snape D, Lane S, et al. Self-reported anxiety and sleep problems in people with epilepsy and their association with quality of life. Epilepsy Behav 2015;43:149–58.
[13] Van Golde EGA, Gutter T, de Weerd AW. Sleep disturbances in people with epilepsy; prevalence, impact and treatment. Sleep Med Rev 2011;15(6):357–68.
[14] van der Meulen WREH Mulder-Hajonides, Wijnberg JR, Hollander JJ, et al. Measurement of subjective sleep quality. Eur. Sleep Res. Soc. 1980;98(5). Abstract.
[15] Meijman T, Thunnissen M, de Vries-Griever AJH. The aftereffects of a prolonged period of day-sleep on subjective sleep quality. Work Stress 1990;4:65–70.
[16] Hays RD, Martin SA, Sesti AM, et al. Psychometric properties of the medical outcomes study sleep measure. Sleep Med 2005;6(1):41–4.
[17] Douglass AB, Bornstein R, Nino-Murcia G, et al. The sleep disorders questionnaire I: creation and multivariate structure of SDQ. Sleep 1994;17(2):160–7.
[18] Sweere Y. The validity of the Dutch sleep disorders questionnaire (SDQ). J Psychosom Res 1998;45(6):549–55.
[19] Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 1991;14(6):540–5.
[20] Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992;15(4):376–81.
[21] Aaronson NK, Muller M, Cohen PDA, et al. Translation, validation, and norming of the Dutch language version of the SF-36 health survey in community and chronic disease populations. J Clin Epidemiol 1998;51(11):1055–68.
[22] van der Heijden PGM, van Buuren S, Fekkes M, et al. Unidimensionality and reliability under Mokken scaling of the Dutch language version of the SF-36. Qual Life Res 2003;12(2):189–98.
[23] Jacoby A, Baker GA, Steen N, et al. The SF-36 as a health status measure for epilepsy: a psychometric assessment. Qual Life Res 1999;8(4):351–64.
[24] Polo-Kantola P. Sleep problems in midlife and beyond. Maturitas 2011;68(3):224–32.
[25] Roth T. Comorbid insomnia: current directions and future challenges. Am J Manag Care 2009;15:S6–13.
[26] Yazdi Z, Sadeghniiat-Haghighi K, Naimian S, et al. Prevalence of sleep disorders and their effects on sleep quality in epileptic patients. Basic Clin Neurosci 2013;4(1):36–41.
[27] Verroti A, Carrozzino Milioni M, et al. Epilepsy and its main psychiatric comorbidities in adults and children. J Neurol Sci 2014;343:23–9.
[28] Reynolds K, Pietrzak RH, El-Gabachiatric R, et al. Prevalence of psychiatric disorders in U.S. Older adults: findings from a nationally representative survey. World Psychiatry 2015:74–81.
[29] Giorelli AS, Passos P, Carnaval T, et al. Excessive daytime sleepiness and epilepsy: a systematic review. Epilepsy Res Treat 2013. https://doi.org/10.1155/2013/629469.
[30] Chen NC, Tsai MH, Chang CC, et al. Sleep quality and daytime sleepiness in patients with epilepsy. Acta Neurol Taiwan 2011;20(4):249–56.