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ORIGINAL RESEARCH

Relationship Between Insomnia and Continued Outpatient Treatment in Psychiatric Patients

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Purpose: Sleep plays an essential role in maintaining both physical and mental well-being. Many patients in psychiatric outpatient settings complain of insomnia. However, the causal relationship between insomnia and depressive symptoms in all mental illnesses remains unclear. Moreover, research on insomnia and the continuation of outpatient treatment is lacking. We hypothesize a high correlation between depression and insomnia among patients with diverse mental illnesses. Additionally, we posit that insomnia significantly influences the continuity of outpatient visits. To this end, we evaluated insomnia and depression symptoms in psychiatric patients both at their initial visit and one year later. We also examined factors related to insomnia at the outset and factors associated with the ongoing utilization of outpatient treatment.

Patients and Methods: The participants of the study consisted of patients who made their first visit to the outpatient department of psychiatry and neurology at Showa University East Hospital between June 1, 2021, and March 31, 2023, and who continued attending the outpatient clinic for one year. Clinical characteristics were assessed using the Self-rating Depression Scale (SDS) and the Athens Insomnia Scale (AIS).

Results: The study's findings were collected from a cohort of 1106 patients and revealed that more than 70% experienced insomnia at the time of their initial visit. In total 137 patients continued to receive outpatient treatment for one year, and their AIS scores improved from 9 points to 5 points. A multivariate analysis revealed that the SDS items of depressed mood and insomnia were confounding factors influencing AIS improvement.

Conclusion: Given that 70% of patients complained of insomnia at the time of their first visit and that sleep improved in many of the 12.4% of patients who continued to receive outpatient treatment for at least one year, the results suggest that sleep status is an important determinant of whether a patient continues to attend outpatient clinics.

Keywords: insomnia, sleep disorder, depression, continuation rate of outpatient treatment

Introduction

Sleep is essential for maintaining physical and mental health; thus, insomnia must be considered in psychiatric outpatient treatment. In a study by Itani et al, 12.2–14.6% of men and women in Japan, respectively, had insomnia.[1] Sleep deprivation can be caused by physiological issues such as sleep apnea syndrome, restless leg syndrome, and periodic limb movement disorder.[2–4] It can also be caused by hormones such as growth hormone, adrenocorticotropic hormone, gonadotropins, and prolactin.[5,6] In psychiatric settings, around 40% of patients with insomnia have a mental disorder,[7] while many mental disorders (including schizophrenia, as well as mood, and personality disorders such as anxiety) are associated with an increased likelihood of insomnia.[8] Evidence also shows that depression increases the risk of insomnia and vice-versa,[9] and that poor quality sleep and nightmares increase the risk of suicidal behavior.[10] However, little is known about the relationship that mental disorders other than depression have with specific depressive symptoms and insomnia.[11] A better understanding of the relationship between each depressive symptom and insomnia could lead to an improved quality of psychiatric care.

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One priority in psychiatric care is to increase the rate of continuing outpatient care. Outpatient care helps prevent relapse and symptom exacerbation, reducing the likelihood that the patient will need to be hospitalized. Despite this, to the best of our knowledge, there are no studies on the portion of patients in Japan who continue making outpatient visits after being diagnosed with a psychiatric disorder. Thus, the impact of continued outpatient visits in the Japanese context remains unknown. In Japan, 48.3% of men and 18.3% of women use alcohol to aid sleep onset at least once a week, while just 4.3% of men and 5.9% of women use sleep medication at least once a week.[12] These findings indicate a strong preference for alcohol over sleep medication as a sleep aid and a strong tendency towards self-medication. Consequently, too few people experiencing disordered sleep receive medical intervention, with less than half seeking advice from a psychiatrist or other medical professional.[13] With such a strong tendency to self-medicate with alcohol, people with insomnia, if they do seek psychiatric care, may be less inclined to continue outpatient visits. One of the reasons patients discontinue outpatient visits is that they feel that the treatment is ineffective. When patients discontinue outpatient visits, the risk for comorbidities increases, and physical problems associated with insomnia can worsen. The physical problems associated with insomnia include conditions such as thyroid problems, acroparesthesia, obesity, hypertension, diabetes, and cardiovascular problems.[14,15] It can also exacerbate mental health symptoms such as depressed mood, decreased motivation, loss of interest, anxiety, decreased appetite, suicidal thoughts, negatively impacting quality of life.[16,17] Therefore, increasing the rate of continuing outpatient care is essential.

Many patients in psychiatric outpatient settings complain of insomnia, while the causal relationship between insomnia and depressive symptoms in all mental illnesses remains unclear. Moreover, research on insomnia and the continuation of outpatient treatment is lacking. However, the reason for the lack of research on the continuation of outpatient treatment is clear: a lack of relevant data. Therefore, we analyzed various data at the start of treatment with the aim of discovering factors that predict treatment continuation. Using available data, we conducted this study to examine the role of outpatient treatment in treating people with insomnia. We hypothesized that depressive symptoms are strongly correlated with insomnia in patients with mental illnesses and that insomnia influences factors relevant to the continuation of outpatient visits, including various symptoms of depression, employment status, sex differences, and prescription drug use. We then evaluated each psychiatric patient's symptoms of depression and insomnia at the time of their first visit and one year later. Finally, factors related to insomnia at the time of their first visit and factors related to the continuation of outpatient treatment were examined and compared.

Study Methods

Participants

We surveyed patients who had made an initial visit to the Outpatient Department of Psychiatry and Neurology at Showa University East Hospital between June 1, 2021, and March 31, 2023. We also surveyed patients who had continued outpatient visits for at least one year following their initial visit. Of the total 1106 patients, 627 were women and 479 were men. The mean age was 44.32 (± 20.59).

Research Design

We obtained data from first-time patients and from a subset of those patients that continued to receive outpatient psychiatric care for one year after the initial visit. First, data from first-time patients were extracted and divided into groups of those with and those without sleep disturbances based on an AIS score of 6 at the initial visit. Next, using data from the first visit of patients who continued treatment for one year, we performed a similar analysis using an AIS score of 6 at one year as the threshold, dividing patients into two groups: those with sleep disturbances and those without sleep disturbances. Therefore, patients only completed an AIS.

Items Studied

Taking a retrospective approach, we prepared a database of patients' age, sex, marital status, years of education, employment status (employed or unemployed), physical comorbidities, diagnosis, prescription, score on the Self-rating Depression Scale (SDS), and score on the Athens Insomnia Scale (AIS). For diagnosis, we used the disorder names listed

in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).[18] ICD-10 categorizes mental and behavioral disorders as follows: F0–F09: Organic, including symptomatic, mental disorders; F10–19: Mental and behavioral disorders due to psychoactive substance use. F20–29: Schizophrenia, schizotypal and delusional disorders; F30–39: Mood [affective] disorders; F40–49: Neurotic, stress-related and somatoform disorders; F50–59: Behavioral syndromes associated with physiological disturbances and physical factors; F60–69: Disorders of adult personality and behavior; F70–79: Mental retardation; F80–89: Disorders of psychological development; F90–99: The onset of behavioral and emotional disorders usually occurs in childhood and adolescence (Table 1). For the initial visit, we considered the following items: age, sex, marital status, years of education, employment status, diagnosis, prescription, SDS score, and AIS score. For >1 year (where the patient had continued attending outpatient care for at least one year from the time of the initial visit), we considered assessment items other than those in the SDS.

Assessment Scales

Self-Rating Depression Scale

A self-administered SDS survey was used to measure the extent to which patients experienced a depressed state. The scale was adapted from the original scale developed by William W.K. Zung in 1965. In the study, we used the Japanese-language version developed by Fukuda et al. It consists of 20 questions about depressed state, each rated on a 4-point scale ("none, or a little of the time", "some of the time", "a good part of the time", "most of the time") to yield a total score ranging from 20 to 80. Scores above 40 indicate a depressed state.

Athens Insomnia Scale

The AIS is an international screening tool for insomnia created as part of the WHO's Worldwide Project on Sleep and Health. The scale consists of an eight-item questionnaire about sleep problems, with responses provided on a three-point scale. If the sleep problem occurred at least three times a week during the past month, the respondent rates the severity of the problem from 0 to 3, for a total score ranging between 0 and 24. A cut-off score of ≥6 indicates insomnia.[19] The Japanese version has been published and validated by Okajima et al.[20]

Analytical Method

In the analysis, we defined age and years of schooling as continuous variables. We defined sex, marital status, employment status, diagnosis, and prescription as categorical variables. We defined both the AIS and SDS scores as continuous variables. For the initial visit, we divided the patients into two groups based on their AIS scores. Patients who scored 5 or less (below the cut-off) were assigned to the Healthy Sleep at Initial Visit group, while those who scored 6 or higher were assigned to the Insomnia at Initial Visit group. We then checked for intergroup differences in the survey items. We performed a multivariate analysis of the two groups to analyze the factors that affect the likelihood of insomnia. For our

Table 1 The ICD-10 Classification of Mental and Behavioural Disorders

F0	**Organic, including symptomatic, mental disorders**
F1	Mental and behavioural disorders due to psychoactive substance use
F2	Schizophrenia, schizotypal and delusional disorders
F3	Mood (affective) disorders
F4	Neurotic, stress-related and somatoform disorders
F5	Behavioural symdromes associated with physiological disturbances and physical factors
F6	Disorders of adult personality and behaviour
F7	Mental retardation
F8	Disorders of psychological development
F9	Behavioural and emotional disorders with onset usually occurring in childhood and adolescence

univariate analysis, we subjected the continuous variables to a *t*-test and the categorical factors to a chi-squared test. For our multivariate analysis, we performed a logistic regression with forced entry, setting the significance threshold at $p > 0.05$.

At >1 year, we divided the patients based on their AIS scores as before. Those with a score of 5 or less were assigned to the Healthy Sleep at >1 Year group, while those with a score of 6 or higher were assigned to the Insomnia at >1 Year group. We then performed a multivariate analysis to check for intergroup differences in the survey items. We subjected the > 1-year AIS scores to univariate analysis using a *t*-test. Using repeated measures ANOVA, we performed a multivariate analysis on change-over-time between the initial visit and >1 year. All statistical operations were computed using SPSS version 22 (SPSS Inc, Tokyo, Japan).

Ethical Considerations

This study complied with the World Medical Association's Declaration of Helsinki and was approved by the ethics committee of Showa University East Hospital (approval number: 22-115-B). We briefed prospective patients on the study's purpose and method, supplied them with contact details, and provided them with an opportunity to opt out of the study to ensure that their consent was informed and freely provided. During the study, we upheld our obligation to safeguard patients' privacy by taking the utmost care to safeguard and maintain the anonymity of their personal information.

Results

Initial Visit

We observed no statistically significant differences attributable to sex, age, years of education, or marital status. However, employment status did prove significant: patients who were employed were significantly more likely than others to have insomnia, as indicated by an AIS score of 6 or higher. Approximately 60% of the initial diagnoses were either "mood [affective] disorders" (F30–39) or "neurotic, stress-related and somatoform disorders" (F40–49). "Organic, including symptomatic, mental disorders" (F0–F09) were associated with a decreased likelihood of insomnia, while "mood [affective] disorder" (F30–39) and "behavioral syndromes associated with physiological disturbances and physical factors" (F50–59) were associated with an increased likelihood of insomnia (Table 2).

Use of sleep medication was significant, with 39% of the patients using prescribed sleep medication. Use of antidepressants was also significant. Patients on antipsychotic medication were more likely than others to experience insomnia.

Insomnia was recognized in over 80% of the patients who were on any of the following types of prescription drugs: benzodiazepines, non-benzodiazepines, or orexin antagonists. AIS scores were higher among patients on antidepressants; likewise, being on antipsychotic drugs was associated with a higher AIS score Tables 3 and 4 shows the results by prescription.

At the initial visit, over 70% of the patients had insomnia, as indicated by an AIS score of 6 or higher (6 being the cut-off) (Figure 1). Comparing insomnia trends at the time of initial diagnosis revealed two disorder categories associated with an increased likelihood of insomnia: Insomnia (AIS score of 6 or higher) was present in 80% of the patients with "insomnia and mood [affective] disorders" (F30–39) and in over 70% of those with "neurotic, stress-related and somatoform disorders" (F40–49). We observed no marked variance in insomnia by diagnosis; each diagnosis category had an insomnia rate above a certain level (Figure 2).

No significant differences in AIS scores were found between the two AIS groups, although the Insomnia at Initial Visit and Healthy Sleep at Initial Visit groups did differ significantly in the first seven of the eight items: Sleep induction, awakenings during the night, final awakening earlier than desired, total sleep duration, overall quality of sleep, sense of well-being during the day, and functioning during the day. Regardless of whether they had insomnia, the patients tended to score high on the eighth item: sleepiness during the day (Figure 3).

Comparing the SDS scores between the two AIS groups showed that patients with insomnia (AIS score of 6 or higher) tended to report having a depressed mood (higher score for "I feel down-hearted and blue"), crying spells (higher score for "I have crying spells or feel like crying"), sleep disturbance (higher score for "I have trouble sleeping at night"), weight loss

Table 2 Patient Baseline Data at Initial Visit

	Initial visit			
	Total (*n* = 1106)	**Healthy Sleep at Initial Visit AIS ≤ 5 (*n* = 301)**	**Insomnia Sleep at Initial Visit AIS>6 (*n* = 805)**	***P* value**
Sex	M: 479 (43.3%) F: 627 (56.7%)	M: 138 (45.8%) F: 163 (54.2%)	M: 341 (42.4%) F: 464 (57.6%)	0.30
Age	44.32 ± 20.59	44.8 ± 22.0	44.2 ± 20.0	0.66
Years of education	13.74 ± 2.45	13.5 ± 2.7	13.8 ± 2.4	0.06
Marital status	Never married: 568 (51.4%) Married or divorced: 538 (48.6%)	Never married: 158 (52.5%) Married or divorced: 143 (47.5%)	Never married: 410 (50.9%) Married or divorced: 395 (49.1%)	0.64
Employment status	Unemployed: 590 (53.3%) Employed: 516 (46.7%)	Unemployed: 186 (61.8%) Employed: 115 (38.2%)	Unemployed: 404 (50.2%) Employed: 401 (59.8%)	< 0.001
Physical comorbidities	172(15.6)	45(15.0)	127(15.8)	0.74
Number of physical comorbidities				
1	151(13.7)	38(12.6)	113(14.0)	
2	18(1.6)	7(2.3)	11(1.4)	
3	2(0.2)	0(0)	2(0.2)	
4	1(0.1)	0(0)	1(0.1)	
F00–F09	79 (7.1%)	39 (13.0%)	40 (5.0%)	< 0.001
F10–F19	32 (2.9%)	8 (3.0%)	24 (3.0%)	0.775
F20–F29	85 (7.7%)	42 (14.0%)	43 (5.3%)	< 0.001
F30–F39	329 (29.7%)	54 (17.9%)	275 (34.2%)	< 0.001
F40–F49	352 (31.8%)	85 (28.2%)	267 (33.2%)	0.117
F50–F59	64 (5.8%)	10 (3.3%)	54 (6.7%)	< 0.05
F60–F69	4 (0.4%)	1 (0.3%)	3 (0.4%)	0.921
F70–F79	21 (1.9%)	13 (4.3%)	8 (1.0%)	< 0.001
F80–F89	24 (2.2%)	10 (3.3%)	14 (1.7%)	0.108
F90–F99	116 (10.5%)	39 (13.0%)	77 (9.6%)	0.101
Pre-AIS total	9.58 ± 5.63	2.97 ± 1.68	12.04 ± 4.49	< 0.001
SDS total score	46.97 ± 6.13	46.7 ± 6.1	47.1 ± 6.14	0.04
40 as cut-off	< cut-off: 87 (7.9%) ≥ cut-off: 1019 (92.1%)	< cut-off: 29 (9.6%) ≥ cut-off: 272 (90.4%)	< cut-off: 58 (7.2%) ≥ cut-off: 747 (92.8%)	0.18
48 as cut-off	< cut-off: 589 (53.3%) ≥ cut-off: 517 (46.7%)	< cut-off: 146 (48.5%) ≥ cut-off: 155 (51.5%)	< cut-off: 443 (55.0%) ≥ cut-off: 362 (45.0%)	0.05
56 as cut-off	< cut-off: 1045 (94.5%) ≥ cut-off: 61 (5.5%)	< cut-off: 292 (97.0%) ≥ cut-off: 9 (3.0%)	< cut-off: 753 (93.5%) ≥ cut-off: 52 (6.5%)	< 0.05

Notes: For diagnosis, we used the disorder names listed in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).
Abbreviations: (SDS), Self-Rating Depression Scale; (AIS), Athens Insomnia Scale.

Table 3 Medications and Sleep Status at Initial Visit

	Initial visit			
	Total (*n* = 1106)	**Healthy Sleep at Initial Visit AIS ≤ 5 (*n* = 301)**	**Insomnia at Initial Visit AIS>6 (*n* = 805)**	***P* value**
Sleep medication: Using?	No: 747 (67.5%) Yes: 359 (32.5%)	No: 257 (85.4%) Yes: 44 (14.6%)	No: 490 (60.9%) Yes: 315 (39.1%)	< 0.001
Sleep medication: Amount used	0.39 ± 0.62	0.13 ± 0.35	0.3 ± 0.51	< 0.001
Orexin sleep medication: Using?	No: 871 (78.8%) Yes: 235 (21.2%)	No: 273 (90.7%) Yes: 28 (9.3%)	No: 598 (74.3%) Yes: 207 (25.7%)	< 0.001
Orexin sleep medication: Amount used	0.21 ± 0.41	0.093 ± 0.29	0.26 ± 0.44	< 0.001
Benzodiazepines sleep medication: Using?	No: 1022 (92.4%) Yes: 84 (7.6%)	No: 289 (96.0%) Yes: 12 (4.0%)	No: 733 (91.1%) Yes: 72 (8.9%)	< 0.05
Benzodiazepines sleep medication: Amount used	0.08 ± 0.28	0.04 ± 0.2	0.09 ± 0.31	< 0.05
Non-benzodiazepines sleep medication: Using?	No: 1030 (93.1%) Yes: 76 (6.9%)	No: 292 (97.0%) Yes: 9 (3.0%)	No: 738 (91.7%) Yes: 67 (8.3%)	< 0.05
Non-benzodiazepines sleep medication: Amount used	0.07 ± 0.26	0.03 ± 0.17	0.09 ± 0.28	< 0.001
Antidepressants: Using?	No: 849 (76.8%) Yes: 257 (23.4%)	No: 262 (87.0%) Yes: 39 (13.0%)	No: 587 (72.9%) Yes: 218 (27.1%)	< 0.001
Antidepressants: Amount used	0.25 ± 0.48	0.13 ± 0.35	0.30 ± 0.51	< 0.001
Anti-anxiety drugs: Using?	No: 942 (85.2%) Yes: 164 (14.8%)	No: 266 (88.4%) Yes: 35 (11.6%)	No: 676 (84.0%) Yes: 129 (16.0%)	0.067
Anti-anxiety drugs: Amount used	0.16 ± 0.40	0.13 ± 0.36	0.17 ± 0.41	0.068
Antipsychotics for schizophrenia: Using?	No: 909 (82.2%) Yes: 197 (17.8%)	No: 244 (81.1%) Yes: 57 (18.9%)	No: 665 (82.6%) Yes: 140 (17.4%)	0.55
Antipsychotics for schizophrenia: Amount used	0.20 ± 0.47	0.23 ± 0.54	0.19 ± 0.45	0.263
Mood stabilizers: Using?	No: 1033 (93.4%) Yes: 73 (6.6%)	No: 280 (93.0%) Yes: 21 (7.0%)	No: 753 (93.5%) Yes: 52 (6.5%)	0.758
Mood stabilizers: Amount used	0.07 ± 0.27	0.07 ± 0.27	0.07 ± 0.27	0.795
Traditional oriental medicine: Using?	No: 1086 (98.2%) Yes: 20 (1.8%)	No: 298 (99.0%) Yes: 3 (1.0%)	No: 788 (97.9%) Yes: 17 (2.1%)	0.215
Traditional oriental medicine: Amount used	0.02 ± 0.14	0.01 ± 0.1	0.02 ± 0.16	0.123
Other antipsychotics: Using?	No: 389 (35.2%) Yes: 717 (64.8%)	No: 149 (49.5%) Yes: 152 (50.5%)	No: 240 (29.8%) Yes: 565 (70.2%)	< 0.001
Other antipsychotics: Amount used	1.20 ± 1.26	0.84 ± 1.1	1.34 ± 1.3	< 0.001

Notes: For diagnosis, we used the disorder names listed in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).
Abbreviations: (SDS), Self-Rating Depression Scale; (AIS), Athens Insomnia Scale.

(higher score for "I notice that I am losing weight"), constipation (higher score for "I have trouble with constipation"), tachycardia (higher score for "my heart beats faster than usual"), fatigue (higher score for "I get tired for no reason"), psychomotor agitation (higher score for "I am restless and can't keep still"), irritability (higher score for "I am more irritable than usual"), and suicidal rumination (higher score for "I feel that others would be better off if I were dead"). The following

Table 4 Medication Usage at Initial Visit

	Total (n = 1106)	Initial visit		
		Healthy Sleep at Initial Visit (AIS ≤ 5)	Insomnia Sleep at Initial Visit (AIS ≥ 6)	p value
Hydroxyzine	2	0 (0%)	2 (100%)	0.387
Dosage	37.5			
Biperiden	10	3 (30%)	7 (70%)	0.842
Dosage	2.1			
Atomoxetine	10	4 (40%)	6 (60%)	0.361
Dosage	48			
Aripiprazole	22	12 (37.5%)	20 (62.5%)	0.185
Dosage	6.87			
Alprazolam	40	12 (30%)	28 (70%)	0.687
Dosage	0.69			
Venlafaxine	15	2 (13.3%)	13 (86.7%)	0.224
Dosage	66.7			
Paliperidone	3	2 (66.7%)	1 (33.3%)	0.124
Dosage	7			
Guanfacine	24	3 (12.5%)	21 (87.5%)	0.102
Dosage	1.5			
Etizolam	16	1 (6.3%)	15 (93.8%)	0.058
Dosage	1.08			
Lormetazepam	6	1 (16.7%)	5 (83.3%)	0.56
Dosage	1.29			
Aripiprazole, long-acting injectable	4	2 (50%)	2 (50%)	0.305
Dosage	400			
Olanzapine	26	7 (26.9%)	19 (73.1%)	0.973
Dosage	6.54			
Chinese medicine: Combination of ginseng, longan, and bupleurum	1	0 (0%)	1 (100%)	0.541
Dosage	7.5			
Chinese medicine: Cinnamon combination plus fossilized bone and oyster shell	2	0 (0%)	2 (100%)	0.387
Dosage	6.25			
Quazepam	1	0 (0%)	1 (100%)	0.541
Dosage	20			

(*Continued*)

Table 4 (Continued).

	Total (n = 1106)	Initial visit		
		Healthy Sleep at Initial Visit (AIS ≤ 5)	Insomnia Sleep at Initial Visit (AIS ≥ 6)	p value
Quetiapine	26	6 (23.6%)	20 (76.9%)	0.631
Dosage	52.3			
Tiapride	1	0 (0%)	1 (100%)	0.541
Dosage	50			
Chlorpromazine	3	1 (33.3%)	2 (66.7%)	0.812
Dosage	45.8			
Clotiazepam	8	2 (25.0%)	6 (75.0%)	0.888
Dosage	8.13			
Clonazepam	5	1 (20%)	4 (80%)	0.716
Dosage	2.1			
Chinese medicine: Poria Five combination	1	0 (0%)	1 (100%)	0.541
Dosage	7.5			
Flutazolam	16	3 (18.8%)	13 (81.3%)	0.443
Dosage	4			
Methylphenidate	7	2 (28.6%)	5 (71.4%)	0.936
Dosage	29.3			
Duloxetine	10	1 (10%)	9 (90%)	0.219
Dosage	30			
Diazepam	5	1 (20%)	4 (80%)	0.716
Dosage	4.6			
Asenapine	6	3 (50%)	3 (50%)	0.209
Dosage	10			
Sulpiride	15	1 (6.7%)	14 (93.3%)	0.072
Dosage	178.1			
Sertraline	24	4 (16.7%)	20 (83.3%)	0.24
Dosage	34.8			
Zopiclone	3	1 (33.3%)	2 (66.7%)	0.812
Dosage	7.5			
Zotepine	2	1 (50%)	1 (50%)	0.469
Dosage	100			

(*Continued*)

Table 4 (Continued).

	Total (n = 1106)	Initial visit		
		Healthy Sleep at Initial Visit (AIS ≤ 5)	Insomnia Sleep at Initial Visit (AIS ≥ 6)	p value
Zolpidem	49	3 (6.1%)	46 (93.9%)	0.001
Dosage	6.67			
Lithium carbonate	21	6 (28.6%)	15 (71.4%)	0.888
Dosage	471.4			
Lemborexant	208	21 (10.1%)	187 (89.9%)	0
Dosage	5.57			
Donepezil	5	4 (80%)	1 (20%)	0.008
Dosage	3.8			
Trazodone	22	2 (9.1%)	20 (90.9%)	0.054
Dosage	31.8			
Vortioxetine	73	7 (9.6%)	66 (90.4%)	0
Dosage	10.2			
Nitrazepam	12	1 (8.3%)	11 (91.7%)	0.139
Dosage	6.83			
Triazolam	9	0 (0%)	9 (100%)	0.065
Dosage	0.25			
Nortriptyline	2	1 (50%)	1 (50%)	0.469
Dosage	27.5			
Paroxetine	8	2 (25%)	6 (75%)	0.888
Dosage	39.4			
Sodium valproate	45	13 (28.9%)	32 (71.1%)	0.797
Dosage	363			
Haloperidol	6	3 (50%)	3 (50%)	0.209
Dosage	5.5			
Chinese medicine: Combination of pinellia and magnolia bark	2	0 (0%)	2 (100%)	0.387
Dosage	6.25			
Quetiapine fumarate	12	4 (33.3%)	8 (66.7%)	0.632
Dosage	96.2			
Perampanel	1	0 (0%)	1 (100%)	0.541

(*Continued*)

Table 4 (Continued).

	Total (n = 1106)	Initial visit		
		Healthy Sleep at Initial Visit (AIS ≤ 5)	Insomnia Sleep at Initial Visit (AIS ≥ 6)	p value
Dosage	2			
Flunitrazepam	27	6 (22.2%)	21 (77.8%)	0.555
Dosage	1.5			
Fluvoxamine	6	2 (33.3%)	4 (66.7%)	0.736
Dosage	71.4			
Brotizolam	32	4 (12.5%)	28 (87.5%)	0.058
Dosage	0.27			
Bromazepam	9	3 (33.3%)	6 (66.7%)	0.679
Dosage	6.06			
Pemoline	6	0 (0%)	6 (100%)	0.133
Dosage	13.3			
Suvorexant	28	7 (25%)	21 (75%)	0.79
Dosage	17.9			
Perospirone	6	2 (33.3%)	4 (66.7%)	0.736
Dosage	5.33			
Chinese medicine: Combination of astragalus, bupleurum, and ginseng	2	0 (0%)	2 (100%)	0.387
Dosage	6.25			
Mirtazapine	58	8 (13.8%)	50 (86.2%)	0.018
Dosage	14.96			
Chinese medicine: Combination of angelica and cyperus	1	0 (0%)	1 (100%)	0.541
Dosage	5			
Chinese medicine: Combination of bupleurum and uncaria	11	3 (27.3%)	8 (72.7%)	0.997
Dosage	6.37			
Lurasidone	29	2 (6.9%)	27 (93.1%)	0.013
Dosage	24.1			
Lamotrigine	11	3 (27.3%)	8 (72.7%)	0.997
Dosage	277.3			
Risperidone	21	9 (42.9%)	12 (57.1%)	0.104
Dosage	3.24			
Clonazepam	15	1 (6.7%)	14 (93.3%)	0.072

(*Continued*)

Table 4 (Continued).

	Total (n = 1106)	Initial visit		
		Healthy Sleep at Initial Visit (AIS ≤ 5)	Insomnia Sleep at Initial Visit (AIS ≥ 6)	p value
Dosage	1.03			
Rilmazafone	1	0 (0%)	1 (100%)	0.541
Dosage	1			
Eszopiclone	25	5 (20%)	20 (80%)	0.412
Dosage	1.8			
Brexpiprazole	21	8 (38.1%)	13 (61.9%)	0.258
Dosage	1.5			
Escitalopram	60	11 (18.3%)	49 (81.7%)	0.112
Dosage	10.3			
Levomepromazine	7	2 (28.6%)	5 (71.4%)	0.936
Dosage	71.3			
Ramelteon	26	2 (7.7%)	24 (92.3%)	0.024
Dosage	7.42			
Blonanserin transdermal patch	48	17 (35.7%)	31 (64.6%)	0.192
Dosage	29.6			
Ethyl loflazepate	33	4 (12.1%)	29 (87.9%)	0.048
Dosage	1.08			
Lorazepam	48	12 (25%)	36 (75%)	0.724
Dosage	0.79			

items were less likely to be associated with insomnia: (depression-related) diurnal variation (higher score for "morning is when I feel the best"), decreased appetite (lower score for "I eat as much as I used to"), decreased libido (lower score for "I still enjoy sex"), confusion (lower score for "my mind is as clear as it used to be"), psychomotor retardation (lower score for "I find it easy to do the things I used to"), hopelessness (lower score for "I feel hopeful about the future"), indecisiveness (lower score for "I find it easy to make decisions"), personal devaluation (lower score for "I feel that I am useful and needed"), dissatisfaction (lower score for "My life is pretty fulfilling"), and emptiness (lower score for "I still enjoy the things I used to do"). Univariate analysis revealed significant variation in item scores but no significant difference in total SDS scores (Figure 4).

Outlined below are the results of the multivariate analysis. The logistic regression revealed that the adjusted odds ratios for being employed (1.72 [95% CI, 1.13–2.62]) and being prescribed sleep medication (2.01 [95% CI, 1.20–3.37]) were significant. Among the SDS items, the significant adjusted odds ratios were as follows: "I feel down-hearted and blue" (1.44 [95% CI, 1.09–1.91]); "Morning is when I feel best" (0.64 [95% CI, 0.51–0.80]); "I have trouble sleeping at night" (3.72 [95% CI, 2.88–4.82]); and "I get tired for no reason" (1.40 [95% CI, 1.11–1.75]). No other items had a significant odds ratio. These results indicated that being employed and taking sleep medication were predictors of insomnia, and the odds ratios for SDS items indicated that patients were more likely to have insomnia (an AIS score of 6 or higher) if they reported depressed mood, no circadian variation, fatigue, and sleep disturbance (Table 5).

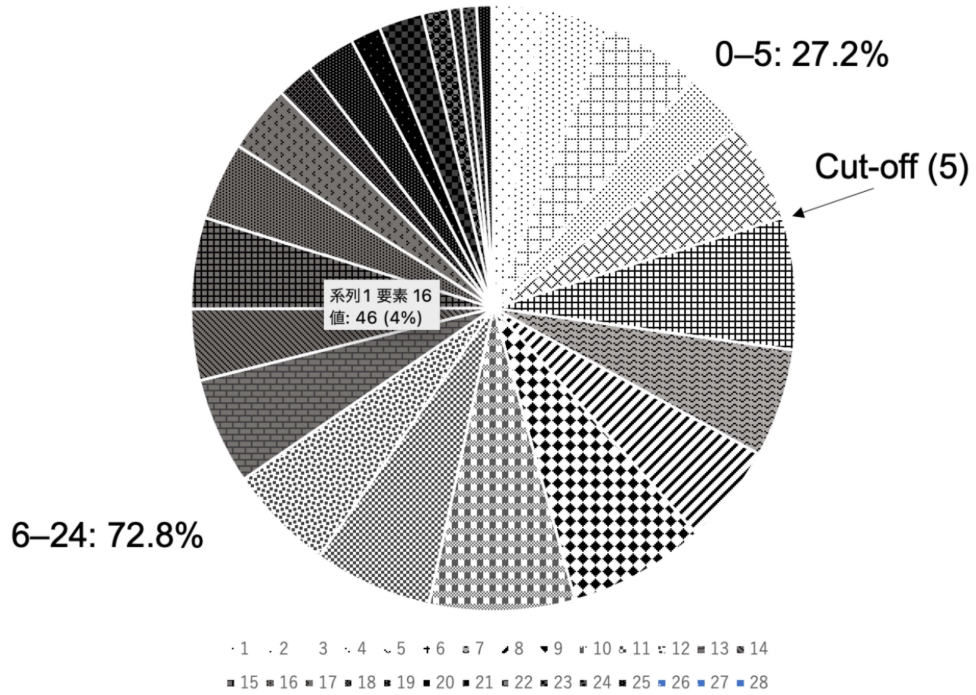

Figure 1 Number of patients by AIS score at initial visit.

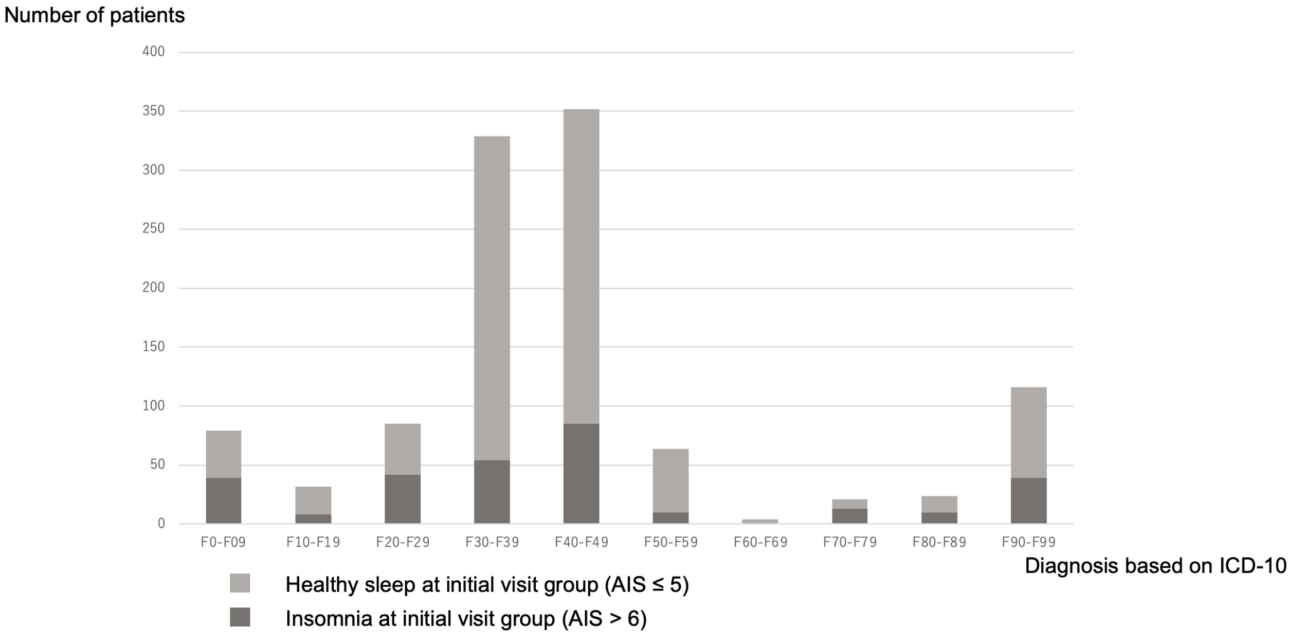

Figure 2 Diagnosis frequency based on ICD-10 by AIS group at initial visit (above or below cut-of).

One Year After Initial Visit

A total of 137 patients (55 men, 82 women; mean age of 45.89 ± 19.12) continued outpatient visits for at least one year after the initial visit. They represented just 12.4% of all patients who had made an initial visit. We observed no noticeable differences in base attributes such as sex between the initial and >1-year visits (Table 6).

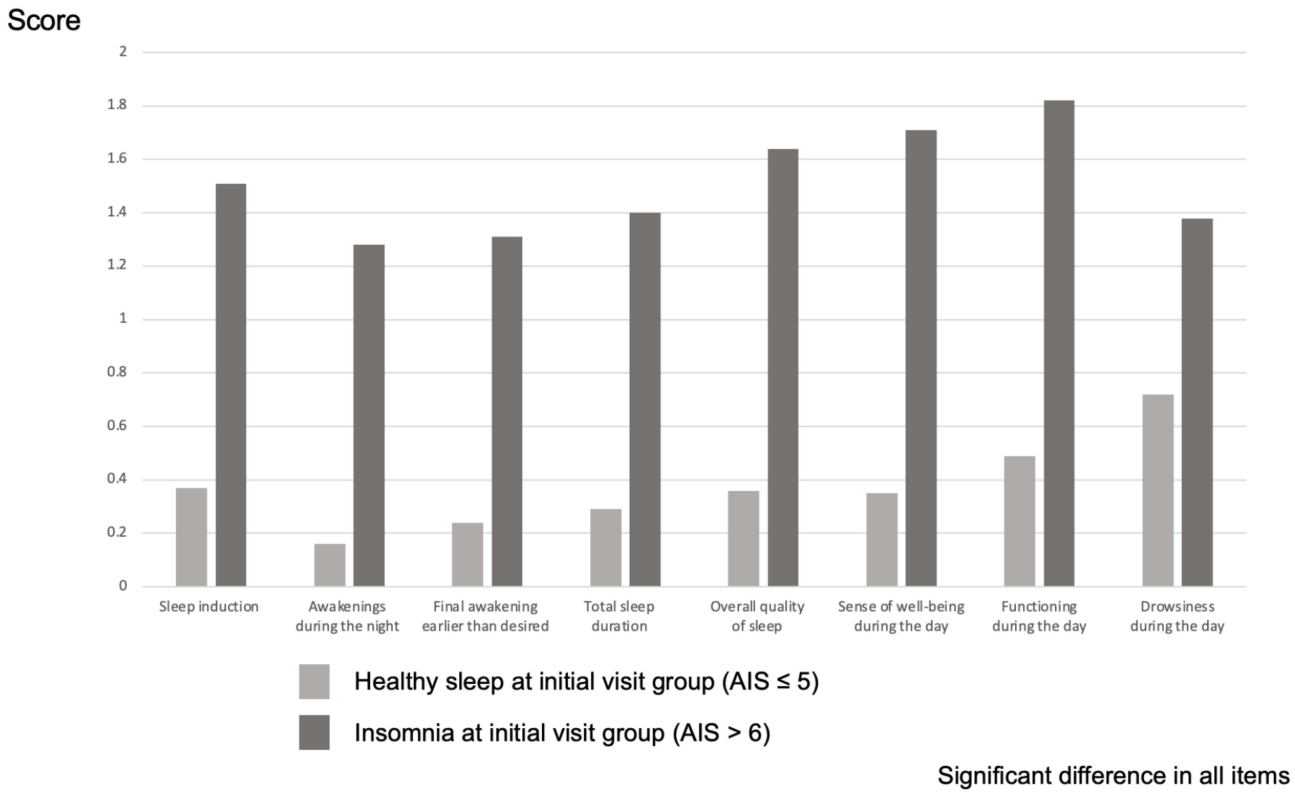

Figure 3 Comparison of AIS item scores between two AIS groups at initial visit.

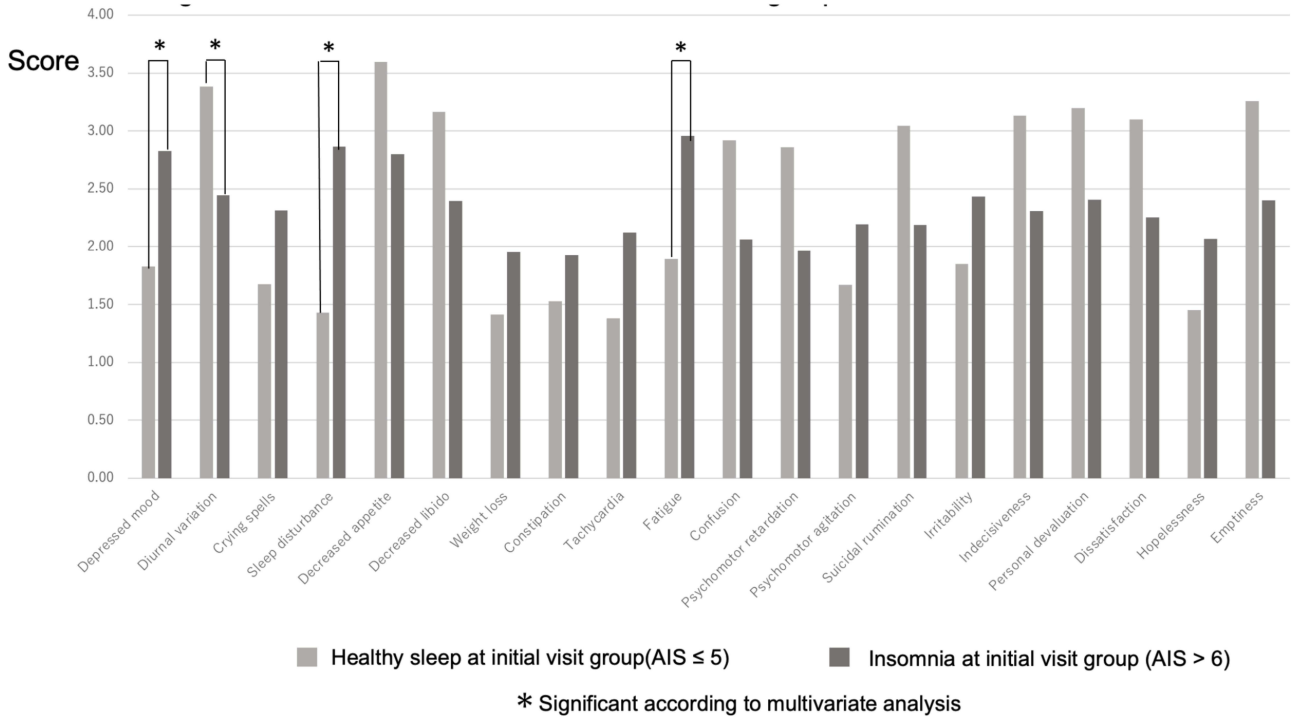

Figure 4 Differences in scores between the two AIS groups at initial visit for each SDS item.

Table 5 Results of Multivariate Analysis

	B	SD	Wald	Degrees of freedom	Exp (B)	95% CI	Significance threshold
Sex	−0.03	0.21	0.21	1	0.97	0.65–1.45	0.87
Marital status	−0.11	0.26	0.26	1	0.90	0.54–1.49	0.67
Employment status	0.54	0.21	0.21	1	1.72	1.13–2.62	< 0.05
F0–F09	−0.24	0.50	0.50	1	0.78	0.30–2.07	0.62
F10–F19	1.14	0.63	0.63	1	3.12	0.91–10.69	0.07
F20–F29	−0.18	0.48	0.48	1	0.84	0.33–2.15	0.71
F30–F39	0.63	0.38	0.38	1	1.88	0.90–3.97	0.09
F40–F49	0.35	0.35	0.35	1	1.42	0.72–2.80	0.31
F50–F59	0.48	0.54	0.54	1	1.62	0.56–4.67	0.37
F60–F69	−1.55	1.39	1.39	1	0.21	0.01–3.23	0.26
F70–F79	−0.38	0.77	0.77	1	0.68	0.15–3.06	0.62
F80–F89	−0.20	0.65	0.65	1	0.82	0.23–2.91	0.76
Antidepressants	−0.02	0.28	0.28	1	0.98	0.57–1.71	0.96
Sleep medication	0.70	0.26	0.26	1	2.01	1.20–3.37	< 0.05
Anti-anxiety drugs	0.18	0.29	0.29	1	1.20	0.68–2.13	0.53
Antipsychotics	−0.46	0.30	0.30	1	0.63	0.35–1.13	0.12
Mood stabilizers	−0.43	0.42	0.42	1	0.65	0.28–1.48	0.30
Traditional oriental medicine	0.65	0.86	0.86	1	1.91	0.36–10.30	0.45
Age	0.01	0.01	0.01	1	1.01	1.00–1.02	0.16
Years of education	0.01	0.04	0.04	1	1.01	0.93–1.10	0.83
Depressed mood	0.37	0.14	0.14	1	1.44	1.09–1.91	< 0.05
Diurnal variation	−0.45	0.11	0.11	1	0.64	0.51–0.80	< 0.001
Crying spells	−0.23	0.13	0.13	1	0.79	0.61–1.02	0.07
Sleep disturbance	1.31	0.13	0.13	1	3.72	2.88–4.82	< 0.001
Decreased appetite	0.01	0.13	0.14	1	1.01	0.78–1.32	0.94
Decreased libido	−0.03	0.10	0.10	1	0.97	0.80–1.17	0.73
Weight loss	0.24	0.13	0.13	1	1.27	1.00–1.64	0.06
Constipation	0.06	0.11	0.11	1	1.07	0.87–1.31	0.54
Tachycardia	0.22	0.13	0.13	1	1.24	0.96–1.61	0.10
Fatigue	0.33	0.12	0.12	1	1.40	1.11–1.75	< 0.05
Confusion	−0.08	0.14	0.14	1	0.92	0.70–1.22	0.55
Psychomotor retardation	−0.02	0.13	0.13	1	0.98	0.76–1.27	0.88

(*Continued*)

Table 5 (Continued).

	B	SD	Wald	Degrees of freedom	Exp (B)	95% CI	Significance threshold
Psychomotor agitation	0.06	0.08	0.08	1	1.06	0.91–1.23	0.48
Hopelessness	−0.01	0.13	0.13	1	0.99	0.77–1.27	0.94
Irritability	0.13	0.12	0.12	1	1.14	0.90–1.45	0.29
Indecisiveness	−0.14	0.14	0.14	1	0.87	0.65–1.15	0.31
Personal devaluation	0.03	0.14	0.14	1	1.03	0.79–1.35	0.83
Dissatisfaction	0.13	0.13	0.13	1	1.14	0.88–1.47	0.33
Suicidal rumination	0.03	0.14	0.14	1	1.03	0.79–1.36	0.82
Emptiness	0.05	0.13	0.13	1	1.05	0.82–1.35	0.70
Constant	−3.79	1.38	1.38	1	0.02		< 0.05

Table 6 Patient Baseline Data at >1-Year Follow-Up

	> 1-year follow-up			
	Total (*n* = 137)	**Healthy Sleep at >1 Year follow-up (AIS ≤ 5) (*n* = 39)**	**Insomnia at >1 Year follow-up (AIS ≥ 6) (*n* = 98)**	***p* value**
Sex	M 55: (40.1%) F: 82 (59.9%)	M: 18 (46.2%) F: 21 (53.8%)	M 37 (37.8%) F 61 (62.2%)	0.37
Age	45.98 ± 19.12	45.1 ± 20.1	47.1 ± 18.0	0.54
Years of education	13.71 ± 2.43	13.9 ± 2.6	13.5 ± 2.2	0.40
Marital status	Never married: 60 (43.8%) Married or divorced: 77 (56.2%)	Never married: 16 (41.0%) Married or divorced: 23 (59.0%)	Never married: 44 (44.9%) Married or divorced: 54 (55.1%)	0.68
Employment status	Unemployed: 77 (56.2%) Employed: 60 (43.8%)	Unemployed: 26 (66.7%) Employed: 13 (33.3%)	Unemployed: 51 (52.0%) Employed: 47 (48.0%)	0.12
Physical comorbidities	24(17.5)	14(18.7)	10(16.1)	0.70
Number of physical comorbidities				
1	23(16.8)	13(17.3)	10(16.1)	
2	1(0.7)	1(1.3)	0(0)	
F0–F09	6 (4.4%)	3 (7.7%)	3 (3.1%)	0.23
F10–F19	2 (1.5%)	0 (0%)	2 (2.0%)	0.37
F20–F29	10 (7.3%)	8 (20.5%)	2 (2.0%)	< 0.001
F30–F39	54 (39.4%)	15 (38.5%)	39 (39.8%)	0.89
F40–F49	47 (34.3%)	9 (23.1%)	38 (38.8%)	0.08
F50–F59	3 (2.2%)	0 (0%)	3 (3.1%)	0.15

(*Continued*)

Table 6 (Continued).

	> 1-year follow-up			
	Total (*n* = 137)	**Healthy Sleep at >1 Year follow-up (AIS ≤ 5) (*n* = 39)**	**Insomnia at >1 Year follow-up (AIS ≥ 6) (*n* = 98)**	***p* value**
F60–F69				
F70–F79				
F80–F89	3 (2.2%)	0 (0%)	3 (3.1%)	0.269
F90–99	10 (7.3%)	4 (10.3%)	6 (6.2%)	0.401
Pre-AIS total	9.66 ± 5.70	8.75 ± 5.75	10.77 ± 5.46	< 0.05
Post-AIS total	5.81 ± 4.46	2.69 ± 1.70	9.58 ± 3.81	< 0.05
SDS total score	48.28 ± 4.87	46.38 ± 3.89	46.24 ± 5.22	0.88
40 as cut-off	< cut-off: 11 (8.0%) ≥ cut-off: 126 (92.0%)	< cut-off: 2 (5.1%) ≥ cut-off: 37 (94.9%)	< cut-off: 9 (9.3%) ≥ cut-off: 89 (90.7%)	0.43
48 as cut-off	< cut-off: 84 (61.3%) ≥ cut-off: 53 (38.7%)	< cut-off: 25 (64.1%) ≥ cut-off: 14 (35.9%)	< cut-off: 59 (60.2%) ≥ cut-off: 39 (39.8%)	0.67
56 as cut-off	< cut-off: 133 (97.0%) ≥ cut-off: 4 (3.0%)	< cut-off: 39 (100.0%) ≥ cut-off: 0 (0%)	< cut-off: 94 (95.9%) ≥ cut-off: 4 (4.1%)	0.2

Notes: For diagnosis, we used the disorder names listed in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).
Abbreviations: (SDS), Self-Rating Depression Scale; (AIS), Athens Insomnia Scale.

Of the patients who had continued their outpatient visits for at least one year, just under 40% had "mood [affective] disorders" (F30–39), and many were on antidepressants. Among the patients with insomnia, sleep medications—particularly orexin antagonists—were prescribed at a high rate (Table 7).

The medications prescribed to patients at >1 year are outlined below (Table 8). Between the initial and >1-year visits, the average AIS score decreased from 9 to 5, denoting a significant improvement in sleep through continued outpatient

Table 7 Medications and Sleep Status at >1-Year Follow-Up

	> 1-year			
	Total (*n* = 137)	**Healthy Sleep at >1 Year follow-up (AIS ≤ 5) (*n* = 39)**	**Insomnia at >1 Year follow-up (AIS ≥ 6) (*n* = 98)**	***p* value**
Sleep medication: Using?	No: 70 (51.1%) Yes: 67 (48.9%)	No: 27 (69.2%) Yes: 12 (30.8%)	No: 43 (43.9%) Yes: 55 (56.1%)	< 0.05
Sleep medication: Amount used	0.57 ± 0.65	0.44 ± 0.55	0.73 ± 0.73	< 0.05
Orexin sleep medication: Using?	No: 96 (70.1%) Yes: 41 (29.9%)	No: 33 (84.6%) Yes: 6 (15.4%)	No: 63 (64.3%) Yes: 35 (35.7%)	< 0.05
Orexin sleep medication: Amount used	0.30 ± 0.46	0.23 ± 0.42	0.39 ± 0.49	< 0.05
Benzodiazepines sleep medication: Using?	No: 119 (86.7%) Yes: 18 (13.3%)	No: 33 (84.6%) Yes: 6 (15.4%)	No: 86 (87.8%) Yes: 12 (12.2%)	0.624
Benzodiazepines sleep medication: Amount used	0.14 ± 0.37	0.16 ± 0.40	0.11 ± 0.32	0.457

(*Continued*)

Table 7 (Continued).

	> 1-year			
	Total (*n* = 137)	**Healthy Sleep at >1 Year follow-up (AIS ≤ 5) (*n* = 39)**	**Insomnia at >1 Year follow-up (AIS ≥ 6) (*n* = 98)**	***p* value**
Non-benzodiazepines sleep medication: Using?	No: 123 (89.8%) Yes: 14 (10.2%)	No: 37 (94.9%) Yes: 2 (5.1%)	No: 86 (87.8%) Yes: 12 (12.2%)	0.215
Non-benzodiazepines sleep medication: Amount used	0.10 ± 0.30	0.04 ± 0.20	0.18 ± 0.39	< 0.05
Antidepressants: Using?	No: 84 (61.3%) Yes: 53 (38.7%)	No: 29 (29.6%) Yes: 10 (70.4%)	No: 55 (56.1%) Yes: 43 (43.9%)	< 0.05
Antidepressants: Amount used	0.42 ± 0.55	045 ± 0.55	0.37 ± 0.55	0.386
Anti-anxiety drugs: Using?	No: 113 (82.5%) Yes: 24 (17.5%)	No: 35 (89.7%) Yes: 4 (10.3%)	No: 78 (79.6%) Yes: 20 (20.4%)	0.158
Anti-anxiety drugs: Amount used	0.18 ± 0.41	0.13 ± 0.34	0.24 ± 0.47	0.12
Antipsychotics for schizophrenia: Using?	No: 96 (70.1%) Yes: 41 (29.9%)	No: 22 (56.4%) Yes: 17 (43.6%)	No: 74 (75.5%) Yes: 24 (24.5%)	0.028
Antipsychotics for schizophrenia: Amount used	0.33 ± 0.57	0.32 ± 0.55	0.34 ± 0.57	0.846
Mood stabilizers: Using?	No: 97 (70.8%) Yes: 20 (29.2%)	No: 31 (79.5%) Yes: 8 (20.5%)	No: 86 (87.8%) Yes: 12 (12.2%)	0.216
Mood stabilizers: Amount used	0.15 ± 0.35	0.13 ± 0.34	0.16 ± 0.37	0.648
Traditional oriental medicine: Using?	No: 135 (98.5%) Yes: 2 (1.5%)	No: 38 (97.4%) Yes: 1 (2.6%)	No: 97 (99.0%) Yes: 1 (1.0%)	0.497
Traditional oriental medicine: Amount used	0.01 ± 0.12	0.03 ± 0.16	0	0.202
Other antipsychotics: Using?	No: 13 (9.5%) Yes: 124 (90.5%)	No: 7 (17.9%) Yes: 32 (82.1%)	No: 6 (6.1%) Yes: 92 (93.9%)	0.033
Other antipsychotics: Amount used	1.83 ± 1.20	1.72 ± 1.15	1.97 ± 1.24	0.227

Notes: For diagnosis, we used the disorder names listed in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).
Abbreviations: (SDS), Self-Rating Depression Scale; (AIS), Athens Insomnia Scale.

visits (Figure 5). Regarding AIS item scores, between the initial and >1-year visits, all item scores improved by approximately 1, except for sleepiness during the day.

Shown below are the changes over time in AIS score in the Healthy Sleep at >1 Year (AIS score of less than 6) group and Insomnia at >1 Year (AIS score of 6 or higher) group. We observed a significant decline (improvement) in average AIS score, at over 7 points, in the Healthy Sleep at >1 Year group, while the score declined only by around 1 in the Insomnia at >1 Year group.

The multivariate analysis (repeated measures ANOVA) indicated two SDS items influenced improvement in AIS score: depressed mood (sum of squared deviations: 137.8; degrees of freedom: 1; F: 8.00, $p < 0.01$) and sleep disturbance (sum of squared deviations: 779.54; degrees of freedom: 1; F: 45.2, $p < 0.01$). We found no direct association among any other factors (eg, sleep medication, employment status). Thus, at the time of initial visit, the "depressed mood" and "sleep disturbance" SDS items predicted improved sleep over a year of continued outpatient visits.

Table 8 Medication Usage at >1-Year Follow-Up

	Total (n = 137)	> 1 year		
		Healthy Sleep at >1 Year follow-up (AIS <6)	Insomnia at >1 Year follow-up (AIS ≥ 6)	p value
Hydroxyzine	1	0 (0%)	1 (100%)	0.527
Dosage			50	
Biperiden	1	1 (100%)	0 (0%)	0.112
Dosage		2		
Atomoxetine	1	1 (100%)	0 (0%)	0.112
Dosage		40		
Aripiprazole	7	4 (57.1%)	3 (42.9%)	0.084
Dosage		5.17	3	
Alprazolam	5	1 (20%)	4 (80%)	0.669
Dosage		0.8	0.4	
Venlafaxine	3	1 (33.3%)	2 (66.7%)	0.85
Dosage		56.3	37.5	
Paliperidone	0			
Dosage				
Guanfacine	5	1 (20%)	4 (80%)	0.669
Dosage		1.75	2	
Etizolam	3	0 (0%)	3 (100%)	0.269
Dosage		1.33	1	
Lormetazepam	1	1 (100%)	0 (0%)	0.112
Dosage		1		
Aripiprazole, long-acting injectable	1	1 (100%)	0 (0%)	0.112
Dosage		400		
Olanzapine	4	2 (50%)	2 (50%)	0.333
Dosage		6.25	7.5	
Chinese medicine: Combination of ginseng, longan, and bupleurum	1	0 (0%)	1 (100%)	0.527
Dosage			7.5	
Chinese medicine: Cinnamon combination plus fossilized bone and oyster shell	0			
Dosage				
Quazepam	1	0 (0%)	1 (100%)	0.527
Dosage			20	

(*Continued*)

Table 8 (Continued).

	Total (n = 137)	> 1 year		
		Healthy Sleep at >1 Year follow-up (AIS <6)	Insomnia at >1 Year follow-up (AIS ≥ 6)	p value
Quetiapine	10	4 (40%)	6 (60%)	0.401
Dosage		71.88	37.5	
Tiapride	0			
Dosage				
Chlorpromazine	0			
Dosage				
Clotiazepam	2	0 (0%)	2 (100%)	0.369
Dosage			10	
Clonazepam	1	1 (100%)	0 (0%)	0.112
Dosage		0.5		
Chinese medicine: Poria Five combination	0			
Dosage				
Flutazolam	2	0 (0%)	2 (100%)	0.369
Dosage			4.5	
Methylphenidate	1	0 (0%)	1 (100%)	0.527
Dosage			45	
Duloxetine	5	0 (0%)	5 (100%)	0.151
Dosage			36	
Diazepam	1	0 (0%)	1 (100%)	0.527
Dosage			2	
Asenapine	0			
Dosage				
Sulpiride	2	0 (0%)	2 (100%)	0.369
Dosage		50	150	
Sertraline	8	1 (12.5%)	7 (87.5%)	0.302
Dosage		40	33.3	
Zopiclone	0			
Dosage				
Zotepine	1	1 (100%)	0 (0%)	0.112
Dosage		150		

(*Continued*)

Table 8 (Continued).

	Total (n = 137)	> 1 year		
		Healthy Sleep at >1 Year follow-up (AIS <6)	Insomnia at >1 Year follow-up (AIS ≥ 6)	p value
Zolpidem	10	0 (0%)	10 (100%)	0.038
Dosage		5	6.88	
Lithium carbonate	6	2 (33.3%)	4 (66.7%)	0.787
Dosage		533.3	500	
Lemborexant	33	4 (12.1%)	29 (87.9%)	0.017
Dosage		5	5.68	
Donepezil	1	1 (100%)	0 (0%)	0.112
Dosage		3		
Trazodone	3	1 (33.3%)	2 (66.7%)	0.85
Dosage		25	25	
Vortioxetine	14	3 (21.4%)	11 (78.6%)	0.538
Dosage		10	10	
Nitrazepam	3	0 (0%)	3 (100%)	0.269
Dosage			8.33	
Triazolam	3	0 (0%)	2 (100%)	0.269
Dosage		0.125	0.208	
Nortriptyline	0			
Dosage				
Paroxetine	2	1 (50%)	1 (50%)	0.497
Dosage			31.3	
Sodium valproate	11	5 (45.5%)	6 (54.5%)	0.193
Dosage		333.3	560	
Haloperidol	2	0 (0%)	2 (100%)	0.369
Dosage			3	
Chinese medicine: Combination of pinellia and magnolia bark	0			
Dosage				
Quetiapine fumarate	5	2 (40%)	3 (60%)	0.56
Dosage		66.7	83.3	
Perampanel	0			
Dosage				

(*Continued*)

Table 8 (Continued).

	Total (n = 137)	> 1 year		
		Healthy Sleep at >1 Year follow-up (AIS <6)	Insomnia at >1 Year follow-up (AIS ≥ 6)	p value
Flunitrazepam	5	3 (60%)	2 (40%)	0.111
Dosage		1.1		
Fluvoxamine	1	0 (0%)	1 (100%)	0.527
Dosage			200	
Brotizolam	6	2 (33.3%)	4 (66.7%)	0.787
Dosage		0.31	0.25	
Bromazepam	1	1 (100%)	0 (0%)	0.112
Dosage		2		
Pemoline	0			
Dosage				
Suvorexant	8	2 (25%)	6 (75%)	0.823
Dosage		18.33	17.5	
Perospirone	1	1 (100%)	0 (0%)	0.112
Dosage		8		
Chinese medicine: Combination of astragalus, bupleurum, and ginseng	0			
Dosage				
Mirtazapine	12	2 (16.7%)	10 (83.3%)	0.343
Dosage		30	18.75	
Chinese medicine: Combination of angelica and cyperus	0			
Dosage				
Chinese medicine: Combination of bupleurum and uncaria	1	1 (100%)	0 (0%)	0.112
Dosage		5		
Lurasidone	4	0 (0%)	4 (100%)	0.2
Dosage			26.7	
Lamotrigine	3	1 (33.3%)	2 (66.7%)	0.85
Dosage		150	400	
Risperidone	6	5 (83.3%)	1 (16.7%)	0.002
Dosage		5.75	1	
Clonazepam	5	0 (0%)	5 (100%)	0.151
Dosage			0.667	

(*Continued*)

Table 8 (Continued).

	Total (n = 137)	> 1 year		
		Healthy Sleep at >1 Year follow-up (AIS <6)	Insomnia at >1 Year follow-up (AIS ≥ 6)	p value
Rilmazafone	0			
Dosage				
Eszopiclone	4	2 (50%)	2 (50%)	0.333
Dosage		2	1.67	
Brexpiprazole	5	3 (60%)	2 (40%)	0.111
Dosage		1.67	1.25	
Escitalopram	9	1 (11.1%)	8 (88.9%)	0.233
Dosage			7.78	
Levomepromazine	1	0 (0%)	1 (100%)	0.527
Dosage			100	
Ramelteon	4	0 (0%)	4 (100%)	0.2
Dosage			5.5	
Blonanserin transdermal patch	5	2 (40%)	3 (60%)	0.56
Dosage		20	20	
Ethyl loflazepate	6	1 (16.7%)	5 (83.3%)	0.512
Dosage		1	1	
Lorazepam	4	1 (25%)	3 (75%)	0.876
Dosage		0.5	0.833	

Discussion

Although as many as 70% of the patients had insomnia, as indicated by an AIS score of 6 or higher, at the time of their initial visit, no conspicuous differences in AIS items were found between the Healthy Sleep at Initial Visit group and Insomnia at Initial Visit group. The multivariate analysis indicated that an AIS score of 6 or higher is associated with being employed and being on sleep medication and is associated with the following SDS items: experiencing depressed mood, having no diurnal variation, experiencing sleep disturbance, and experiencing fatigue. After a year of continued outpatient visits, patients' scores decreased (improved) from an average of 9 to 5 in eight of the nine AIS items. Our multivariate analysis also indicated that two SDS items—depressed mood and sleep disturbance—influenced sleep improvement.

We were unsurprised to find a strong association between insomnia and depressed mood but were surprised to find that insomnia improved among the patients who continued their outpatient visits. This trend was particularly notable in patients with depressed moods at the initial visit; among these patients, the average AIS score declined (improved) to 5 or below after a year of continued outpatient visits. This trend underscores the need to consider depressed mood in treating insomnia. Our findings regarding the relationship between depressed mood and insomnia align with previous studies.

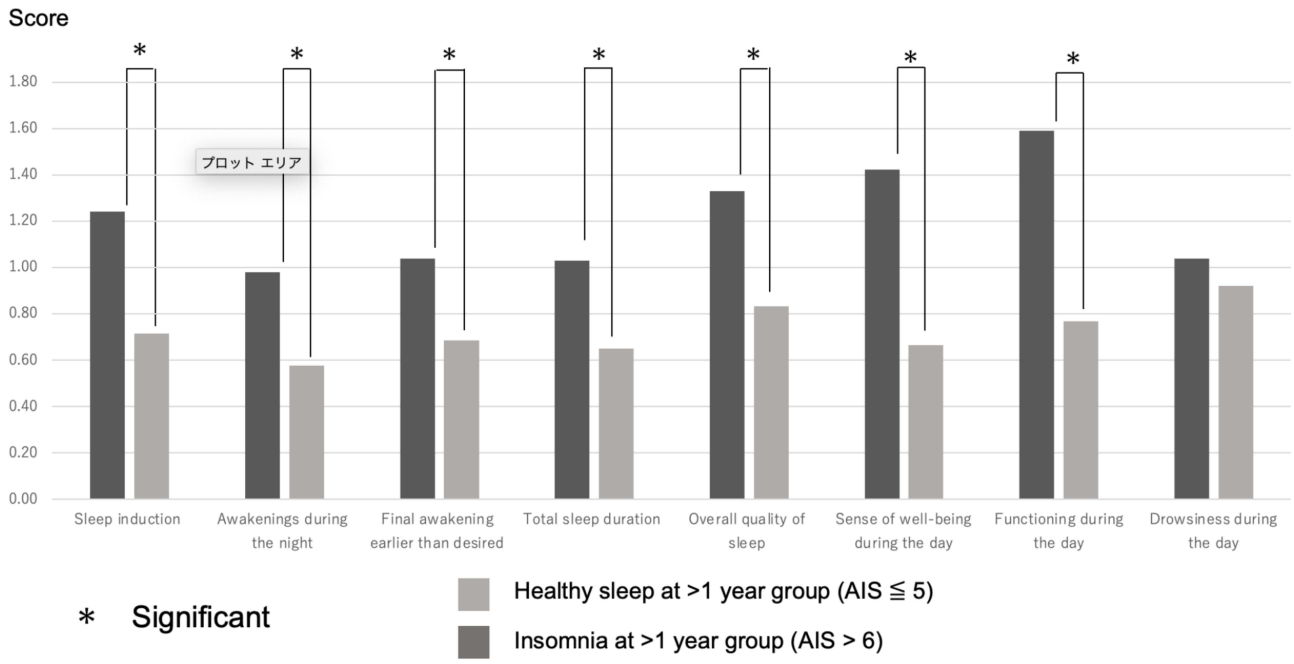

Figure 5 Comparison of AIS item scores at initial visit and >1 year.

One study reported that 77–90% of people with depressive disorder experience insomnia, and 40%, 30%, and 30% experienced insomnia before, during, and after an initial depressive episode, respectively.[21] Among those who experienced subsequent depressive episodes, approximately 20% experienced insomnia after the episode. Thus, depressed mood is a useful predictor of insomnia. Another study reported that patients with depression had a 6.7 odds ratio for subsequently experiencing insomnia.[22] Our analysis showed that a higher (worse) SDS score for depressed mood was associated with an increased likelihood of insomnia. This finding implies that adequate screening during the initial visit and early intervention for insomnia can help prevent the patient's psychiatric symptoms from worsening. Our analysis indicated no statistically significant differences by diagnosis, implying that treating comorbid depression and insomnia is essential regardless of the underlying disease.

Our analysis indicated that employment status and use of antipsychotics were associated with insomnia at the initial visit. However, sex had no such association. Employment status and use of antipsychotics were not associated with an improvement in sleep after a year of continued outpatient visits. The literature suggests that insomnia is associated with high work-related stress, disparate efforts in work and leisure, high demand, heavy workload, and low social support.[23] "Fatigue/malaise", one of the diagnostic criteria of insomnia in the International Classification of Sleep Disorders, can impede functioning during the day.[24] Our results showed that fatigue was associated with insomnia. Thus, interventions for insomnia are essential for addressing presenteeism—when workers attend work but have diminished efficiency and productivity and undermine workplace safety. The literature suggests that sex differences play a role: Among women who experience premenstrual syndrome experience, over 70% experience an impact in their daily life as a result of insomnia and other physical symptoms;[25] insomnia during pregnancy increases the risks for premature birth and depression;[26] among postmenopausal women, 35–60% experience sleep disorder;[27] women aged in their 40s or 50s experience higher production of orexin as a result of a decline in estrogen levels amid diminished ovarian function;[28,29] among women who experience a menopause-related decline in progesterone production (which stimulates the respiratory center, increasing breathing rate),[30] sleep apnea syndrome is approximately as prevalent as it is among men (whereas among other women, it is less prevalent than among men).[31] While our study revealed no significant sex-based differences, women outnumbered men at the initial visit and at >1 year, and the mean age, 44, suggested that many patients would have been experiencing menopause; thus, sex should be taken into account during medical checks. Regarding the medications that the patients were prescribed at their initial visit, around 30% were sleep medications. Of

these medications, over 60% were orexin antagonists. At >1 year, orexin antagonists accounted for over 60% of the sleep medications being prescribed. This result may suggest an increasing preference for orexin antagonists as a pharmaceutical treatment for primary insomnia amid concerns about the harmful effects of benzodiazepines (including dependency and risk of falling).[32] In clinical practice, there are international sleep guidelines that are practical and useful for physicians, such as the European Insomnia Guideline and Clinical Practice Guidelines of the American Academy of Sleep Medicine clinical practice guideline.[33–35] While the guidelines do not recommend prescribing antidepressants for insomnia only (insomnia being outside the indications),[36] mirtazapine (a sedative antidepressant) is frequently prescribed for comorbid insomnia and depressed mood. However, we found that the average AIS score declined (improved) from 9 to 5 points over a year of continued outpatient visits, implying that outpatient visits concerning depressed mood can facilitate improvements in sleep. While we found no statistically significant differences by medication, the possibility remains that orexin antagonists and other sleep and depression medications may have affected the outcomes. Non-pharmaceutical outpatient interventions may have also helped improve sleep outcomes; these interventions would have included guidance in daily life (regarding sleep environment, exercise, diet, smoking, and drinking), cognitive-behavioral therapy, and psychotherapy. Thus, outpatient psychiatric treatment can address sleep problems while also affecting depressed mood, regardless of whether the patient has an underlying disease other than a mood disorder.

We predicted that physical comorbidities would affect sleep and depressive symptoms, but this relationship was not found in this study. Physical comorbidities ranged from sleep apnea and restless legs syndrome, defined as sleep disorders, to cancer, bronchial asthma, Graves' disease, lumbar spinal canal stenosis, endometriosis, and benign prostatic hyperplasia. It has been reported that patients with physical complications are more likely to have sleep disturbances and depression. Considering the results of this study, it is possible that the patients were from a general hospital with a physical treatment department and had received adequate physical treatment, resulting in the less negative impact on their sleep. It is important for the relationship between physical comorbidities and insomnia to be studied further.

Of the patients who made an initial visit to the outpatient clinic, 12.4% continued visiting the clinic for a year. Of the patients who did not continue visiting the clinic for a year, some may have discontinued their visits because their symptoms had improved, while others may have resumed visits to the hospital that had referred them to the clinic. We did not consider the rate of outpatient continuance by disease diagnosis, but it seems likely that continuance rates varied by disease. While outpatient continuance does not necessarily correspond to patient adherence, Semahegn A et al suggests that approximately 50% of patients discontinue treatment, with adherence rates of 49% among patients on antipsychotics, 50% among patients with depression, and 52% among patients with insomnia.[37] Only 12.4% of the patients in our study continued their visits for at least a year, but patients who continued outpatient visits experienced improved sleep. The hospital in our study treats many outpatients with mood disorders and mental health problems and prescribes sleeping medication in up to 50% of the cases, which might explain the significant improvement in AIS score. While it is important to treat comorbid psychiatric conditions, our results show that treating insomnia leads to improvements not only in psychiatric symptoms but also in overall quality of life. When patients experience increased satisfaction with treatment, they are more likely to continue their outpatient visits, increasing their prospects of receiving adequate treatment for the underlying psychiatric or physical condition.

Our study had several limitations. First, the study was restricted to an urban area, meaning that it did not fully consider differences in sleeping issues between urban and rural environments. Second, the study was limited to a university hospital, meaning that it had a high number of cases that are less likely to be diagnosed in private practice and cases involving conditions that co-occur with severe physical conditions. As such, the trends we observed among the patients making their first visit may differ from those that we would have observed in a more typical psychiatric hospital. Therefore, our findings may not be generalizable to patients in other hospitals. Patients may be less likely to continue outpatient visits at university hospitals because attending physicians often take over the case. Third, we used self-administered questionnaires to gather data. In these questionnaires, the patients reported their subjective impression of their condition, which may not align with an objective diagnosis or objective evaluation. Fourth, the severity and treatment status of physical comorbidities were not examined in detail. Fifth, our sample of patients who continued outpatient visits for a year was small, and we did not measure depression in patients at >1 year. The final limitation concerns our comparison of the healthy sleep and insomnia groups at >1 year; because we never compared outcomes between these patients and patients who discontinued outpatient visits, any conclusion drawn from the comparison is speculative.

Data from patients not continuing treatment after one year should be compared to examine factors contributing to treatment continuation. The results of this study do not prove that the effects of specific sleep medications or psychiatric treatments are directly related to improvements in sleep and may change over time. However, the design of this study was unavoidable because it is difficult and impractical to obtain data from patients who do not present themselves at the hospital. While this design may not be entirely appropriate, we speculated that data from the initial visit might predict factors that would help patients continue treatment up to one year later. Sleep status is, nonetheless, likely a significant determinant of whether a patient will continue outpatient visits, given that 70% of the patients had complained of insomnia at their initial visit and that sleep improved in many of the 12.4% of patients who continued their outpatient visits for at least a year. When we performed a multivariate analysis, dividing the patients based on their AIS scores (5 or less versus 6 or more), we were intrigued to find that the presence of depressed mood at the initial visit facilitated an improvement in sleep at >1 year. We suggested earlier that the patients may have experienced an improvement in their depressed mood. To investigate this possibility, it is necessary to compare outcomes with those in patients who discontinued outpatient visits and to use the SDS at >1 year (instead of just at the initial visit). Thus, to further examine the relationship between insomnia and depression, it is necessary to track outcomes over an extended period to account for factors such as the risk of a relapse into a depressive episode.

Conclusion

We found that many psychiatric patients complained of insomnia during their initial visit and that their insomnia was related to their background psychiatric condition. The results suggest that improving insomnia makes patients more likely to continue their outpatient visits, thereby helping prevent secondary mental symptoms and physical problems.

Abbreviations

(SDS), Self-rating Depression Scale; (AIS), Athens Insomnia Scale; (ICD-10), International Statistical Classification of Diseases and Related Health Problems.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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