Hartz et al.[16] examined risk factors for insomnia subtypes by using a cross-sectional survey and concluded that every insomnia subtype is strongly associated with depressive symptoms. Rodin et al.[17] stated EMA was more closely related to depression than three other sleep problems, including difficulty falling asleep. Although Rodin et al. collected longitudinal data to examine the relationship between sleep disturbances and depression, their analyses of the relationship were basically cross-sectional in nature. Their analyses suggested that "in the same subject, a decrease in depression is associated with a corresponding decrease in early morning awakening."

Nevertheless, two recent large-scale epidemiological studies in Japan yielded quite different results concerning the relationship between depression and subtypes of insomnia. Using the CES-D to elucidate the relationship of depression to insomnia, Kaneita et al. evaluated 24,686 people (aged ≥ 20 years) throughout Japan for depression.[2] Sukegawa et al. studied 2,023 residents aged ≥ 65 years in one city using the Geriatric Depression Scale and Pittsburgh Sleep Quality Index.[18] These studies, both of which used questionnaire surveys based on self-rated responses, reported that the closest connection to depression was found not with EMA or DMS, but with DIS. Being cross-sectional studies, however, they could not adequately explore the causal relationship between insomnia subtypes and the presence of depression. We therefore, employed a longitudinal survey on elderly Japanese to examine the temporal association between insomnia subtypes and the presence of depression three years later.

PARTICIPANTS AND METHODS

Selection of Participants

Nihon University has been conducting a nationally representative longitudinal survey on elderly Japanese since 1999 (Nihon University Japanese Longitudinal Study of Aging: NUJLSOA).[19] Six thousand seven hundred elderly Japanese aged ≥ 65 years were sampled by a multistage stratified sampling method in conformity with the population composition at the time. Four thousand nine hundred ninety-seven participants gave informed consent (74.6% retrieval). They were visited and interviewed by well-trained interviewers. Participants aged ≥ 75 years were oversampled by a factor of 2 so that the data for this age group could be analyzed in detail. All the numbers reported in the results are weighted values.

The survey was repeated on the same cohort in 2001, 2003, and 2006, with sample refreshing in 2001 and 2003 for those aged 65 and 66. The present study was based on the 2003 data (number of participants excluding proxy respondents: 4,028) consisting of 1,765 males (45.0%) and 2,263 females (55.0%). All of these participants were included in our cross-sectional studies. Of those, 3,065 without depression in 2003 were included in our longitudinal analyses. We excluded those who had died by the time the 4th survey was conducted in 2006 and those whose responses to the interview were in any way incomplete. The present study employs surveys conducted in 2003 and 2006 because questions on sleep disturbances were only first introduced in the survey conducted in 2003 as a module and kept in the survey conducted in 2006.

Measures

The relationship between the presence of depression and insomnia subtypes was examined by controlling for sleep related, sociodemographic, and health-related factors in the multivariate analyses in our study. Depression, a dependent variable of our study, was evaluated by means of the 11-item short form of the Center for Epidemiological Studies Depression (CES-D) Scale, which had been proposed by Kohout et al.[20] from the 20-item standard form CES-D, developed by Radloff.[21] The time frame of the CES-D is over the previous one week. Shima et al.[22] have confirmed the reliability and validity of the Japanese version of the 20-item standard form, for which they proposed 16 as a reasonable cut-off point. The cut-off point, reliability, and validity of the Japanese version of the 11-item CES-D scale used in this study has been examined and reported by Yokoyama et al.[23] The cut-off point for the 11-item CES-D scale was estimated at 7, equivalent to the cut-off point of 16 for the Japanese version of the standard 20-item CES-D scale. In the present study, those with a score ≥ 7 were defined as having depression.

Sleeping problems, including three insomnia symptoms, were measured by self-reported responses to 5 questions utilized by previous studies.[24-26] The five questions used in the survey are the following:

1) Difficulty initiating sleep (DIS): "Do you have difficulty falling asleep at night?"
2) Early morning awakening (EMA): "Do you wake up too early in the morning and have difficulty getting back to sleep?"
3) Difficulty maintaining sleep (DMS): "Do you wake up during the night after you have gone to sleep?"
4) Excessive daytime sleepiness (EDS): "Do you feel excessively sleepy during the daytime?"[27]
5) Discomfort feeling in the legs (DFL): "Is your sleep interrupted by an itchiness (creeping sensation) or burning sensation in your legs after you go to bed at night?"[28,29]

There are five response categories for these questions: 1, never; 2, seldom; 3, sometimes; 4, often; and 5, always. Those who responded 1 to 3 to the questions were regarded as not having the particular sleeping problem, and those who responded 4 and 5 as having the particular sleeping problem. Insomnia (ANY as a variable name in the tables) was defined, according to a previous study,[25] as the condition that resulted in the participant reporting the presence of at least one of the symptoms: DIS, DMS, and EMA.

In addition, two more sleep related variables were controlled for in this study. Subjective sleep sufficiency was examined with the question: "When you wake up in the morning, how often do you feel that you have had a good night's rest?" Response categories to this question are the same as those for insomnia symptoms. Those who responded "never" and "seldom" were regarded as having had insufficient sleep, and those who chose one of the three other responses as having had sufficient sleep. This question is the flip side of the question on non-restorative sleep.

Sleep duration was evaluated by the self-reported response to the question: "How many hours do you sleep a day on average?" The responses were classified into 5 categories (< 6 h; ≥ 6 to < 7 h; ≥ 7 to < 8 h; ≥ 8 to < 9 h; ≥ 9 h) and analyzed. Kaneita et al.[2] showed the effect of sleep duration on depression as taking on a U-shape, with the bottom at about 7 hours.

Sociodemographic factors including age, gender, educational history, and present place of residence (rural vs. urban dwellers) were controlled for as in most of the previous studies examining the relationship between depression and insomnia. This is because studies have shown that the prevalence of depression and insomnia increases as age increases, and tends to be higher for females.[2,15,16] Many previous studies of the relationship between insomnia and depression have also controlled for educational history[2,15,16] and current place of residence.[15]

For analyses, age was treated as a categorical variable. Four dummy variables were created for each 5-year age group: that is 70-74, 75-79, 80-84, and ≥ 85. Those aged 65-69 were the reference age group. Educational history was classified into two groups (junior high school or less, and high school or more). The present place of residence was subdivided into two groups, urban and rural, the former denoting cities and towns, and the latter referring to areas engaged in farming, forestry, and fishing.

Three health-related factors were also controlled for in the present study. Previous studies have indicated a higher prevalence of depression among those with psychological stress,[7] poor self-rated health,[30] and activities of daily living (ADL) difficulties.[31,32] Participants were asked if they had psychological stress in their daily life. This required either a "yes" or "no" answer.

Participants were asked about their self-rated health with the question: "How do you rate your present general health condition: 1 excellent; 2 good; 3 fair; 4 poor; 5 very poor?" Their responses were grouped into 3 categories: 1 and 2 as good, 3 as fair, and 4 and 5 as poor.[33] Two dummy variables were created for good and poor, and fair was treated as the reference group in the analyses.

For ADL, participants were asked if the following seven activities were difficult or not difficult to perform: bathing, eating, dressing, getting in and out of bed or chairs, walking inside the house, going outside, and using a toilet. Participants with at least one difficulty were classified as having difficulty.

The study procedure was approved by the Ethics Committee of Nihon University.

Statistical Analyses

First, we computed Pearson correlation coefficient among the three insomnia symptoms (i.e., DIS, EMA, and DMS) in order to examine the relationship among them. The correlation was computed for all the participants, including those without depression at the time of the 3rd survey conducted in 2003.

We examined statistically the association of insomnia with the presence of depression. Comparison was made by using the mean CES-D scores computed for those who were identified as having depression and those who were not. Comparisons of 2 categories were performed with the unpaired Student *t*-test, and comparisons of ≥ 3 categories were performed with one-way ANOVA and the Tukey method of multiple comparison.

The relationship between depression and insomnia symptoms was analyzed on the basis of univariate and multivariate logistic regressions. The cross-sectional study using data from the 3rd survey of NUJLSOA (2003) was conducted by a series of logistic regression analyses. The longitudinal study was conducted only on those without depression in 2003. Insomnia variables in 2003 were then regressed on the presence of depression in 2006, controlling for age, gender, educational history, place of residence, sleep duration, EDS, DFL, subjective sleep sufficiency, psychological stress, self-rated health, and ADL.

Table 1— Comparison of age groups between present study and census data

	Age (y)				
	65-69	70-74	75-79	80-84	85+
Present study in 2003					
Total (%)	32.8	25.2	19.5	13.9	8.7
Men (%)	34.7	27.8	19.0	11.7	6.8
Women (%)	31.2	23.1	19.8	15.6	10.3
Census data in 2000					
Total (%)	32.3	26.8	18.9	11.8	10.1

Values given are percentage in age group. All the numbers listed in Table 1 and onward are weighted so they resemble the extracted values from the population composition and not integers.

The 11-item CES-D scale includes the question on whether sleep was restless. In analyzing the relationship between depression and sleeping problems, a possible bias, especially for cross-sectional analyses, may be introduced by including the sleep-related question in the CES-D scale. We therefore conducted additional analyses with the 10-item CES-D scale, excluding this question. By applying a regression equation, following the method of Kohout et al.,[20] the cut-off point for the 10-item CES-D scale was estimated at 6.5. Because the cut-off points have to be an integer number, scores of 6 and 7 were used to evaluate the relationship between insomnia subtypes and the presence of depression. To evaluate possible biases, both the cross-sectional and longitudinal study were repeated for the presence of depression defined by the 10-item short form of the CES-D scale with the cut-off points of 6 and 7 in order, but excluding the sleep item question.

Statistical analyses were performed with SAS 9.1.[34] The statistical level of significance was $P < 0.05$ (two-sided tests).

RESULTS

Demographic Characteristics

Table 1 compares the age-bracketed proportional composition of elderly Japanese in the third survey conducted in 2003 and in the census data of 2000. The proportional composition at the baseline was similar to that in the census data in all age brackets except for the ≥ 85 bracket, where data used for this study were slightly lower. The average age and standard deviation (minimum to maximum) for the participants were 73.1 ± 6.4 (65 to 99) for 2003 and 75.7 ± 6.1 (67 to 103) for 2006.

Correlation among Insomnia Subtypes

Correlation coefficients among the 3 insomnia subtypes are shown in Table 2. Numbers in the upper triangle correspond to all participants and numbers in the lower triangle correspond to those without depression in the third survey conducted in 2003. The correlation was relatively higher for all the participants of the survey compared to those without depression. In all cases, the Pearson correlation coefficients are < 0.4, and the

Table 2—Pearson correlation coefficient among insomnia subtypes: 2003

Insomnia subtype	DIS	EMA	DMS
DIS	-	0.383*	0.309*
EMA	0.282*	-	0.358*
DMS	0.248*	0.321*	-

Numbers in the upper triangle are based on all participants (N ≅ 4,000). Numbers in the lower triangle are based on participants without depression (N ≅ 3,050). DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep. *Statistically significant at 0.01 level.

relationship among the 3 insomnia subtypes is considered to be relatively weak.

Prevalence of Insomnia Symptoms and Depression

Table 3 compares participants' attributes. When estimated by means of the 11-item short form CES-D scale, the presence of depression among elderly Japanese (≥ 65 years) stood at 13.8%, as shown in the first line of Table 3. Overall prevalence of insomnia (ANY) for the sample was 27.8%. The prevalence of insomnia subtypes from highest to lowest is as follows: DMS (22.9%); EMA (11.5%); DIS (11.1%). Prevalence of sleep disturbances was 8.1% for EDS and 3.7% for DFL. Overall, 16.8% of elderly Japanese reported subjective insufficient sleep.

The prevalence of depression in the insomnia symptom groups was: DIS (34.8%); EMA (29.1%); and DMS (20.2%). Each insomnia symptom had significantly different average CES-D scores. DIS had the highest average "yes" responses. Elderly Japanese with EDS, DFL, and subjective insufficient sleep seemed to report a relatively higher prevalence of depression: 28.1%, 24.4%, and 23.3%, respectively.

Relationship between Insomnia Symptoms and Depression

Table 4 shows results of the cross-sectional and longitudinal study on the relationship between insomnia (defined as having any one of the insomnia subtypes) and depression in both univariate and multivariate analyses, thereby allowing a comparison of results from previously conducted studies. For multivariate analyses, sleep related, sociodemographic, and health-related factors were controlled. In the cross-sectional study, insomnia (ANY) was statistically significantly related to the presence of depression in both univariate (OR: 2.217 with 95% CI 1.832 to 2.682) and multivariate analyses (aOR: 1.272 with 95% CI 1.000 to 1.618). However, in the longitudinal study, insomnia (ANY) was significant only at 0.1 level in the multivariate analysis (aOR: 1.293 with 95% CI 0.959 to 1.744), while controlling for sleep related, sociodemographic, and health related factors.

Table 5 illustrates the results of the cross-sectional study involving all participants of the third survey. Using a univariate analysis, all insomnia symptoms were found to be significantly related to the presence of depression. The multivariate analysis, on the other hand, demonstrated that only DIS and EMA had a significant relationship to the presence of depression, after controlling for age, gender, educational history, place of residence, sleep duration, EDS, DFL, subjective sleep sufficiency, psychological stress, self-rated health, and ADL. The adjusted odds ratios (95% CI) were 2.020 (1.455 to 2.805) and 1.441 (1.025 to 2.026), respectively.

Table 6 represents the results of the longitudinal study of those without depression in 2003. The presence of depression in 2006 in the participants who had not been suffering from the disease at the time of the 3rd survey was regarded as the response variable and insomnia symptoms as the explanatory variables, after controlling for sleep related, sociodemographic, and health-related factors. DIS, EMA, and DMS were all shown to be significantly related to depression in the univariate analysis; but in the multivariate analysis DIS was the only symptom with a significant relationship to the presence of depression, with an adjusted odds ratio (95% CI) of 1.592 (1.012 to 2.504).

It is worth mentioning that the results indicate that gender, stress, and self-rated health among the control variables had statistically significant effects on the presence of depression. The effect of psychological stress was substantively about the same as DIS with an adjusted odds ratio (95% CI) of 1.553 (1.125 to 2.145). Those who reported their health as poor at the baseline survey were more likely to have depression in the following survey with an adjusted odds ratio (95% CI) of 2.517 (1.778 to 3.562).

In addition, we examined the relationship between the presence of depression and the insomnia subtypes by controlling for the baseline participants' CES-D scores that vary from 0 to 6 with other control variables. The result of this analysis (not shown) differed slightly from the result shown in Table 6. The adjusted odds ratios (95% CI) for DIS, EMA, and DMS were 1.509 (0.957 to 2.381), 1.023 (0.634 to 1.651), and 1.206 (0.853 to 1.706), respectively. Although the significance level of the effect of DIS on depression was slightly affected by controlling for the CES-D score at baseline, the general tendency of the effect of insomnia subtypes was not affected.

Comparison of the Sleep-Item-Excluded 10-Item CES-D Scale with the 11-Item CES-D Scale

The results of the cross-sectional and longitudinal analyses were re-examined based on the 10-item CES-D scale, which, excluding the sleep item, is the 11-item short form of CES-D with 2 different cut-off points (6 and 7). As shown in Table 7, the adjusted odds ratios in the cross-sectional analyses (95% CI) were 1.819 (1.327 to 2.493) for DIS with the cut-off point of 6, and 1.721 (1.214 to 2.439) with the cut-off point of 7. For EMA, the adjusted odds ratios (95% CI) were 1.262 (0.910 to 1.748) with the cut-off point of 6, and 1.476 (1.030 to 2.114) with the cut-off point of 7. In the longitudinal analyses, the adjusted odds ratios (95% CI) were 1.659 (1.047 to 2.629) for DIS with the cut-off point of 6, and 1.444 (0.936 to 2.227) with the cut-off point of 7. Although there are slight differences between the 10-item scale and the 11-item scale, the general tendency appears to be similar.

From the cross-sectional analyses, DIS and EMA appeared to be associated with the presence of depression. Only DIS, however, demonstrated a significant relationship to the development of depression with the cut-off point of 6 when the sleep item was removed from the 11-item short form of the CES-D Scale.

Table 3—Sample distribution, prevalence of depression and mean CES-D scores by categories of sample attributes and self-reported responses, and results of statistical test for mean CES-D scores among categories in 2003

Baseline items in 2003 Category	Percentage of category (%)	Prevalence of depression* (%)	11-item short forms of the CES-D score (mean ± SD)	Statistical test for mean CES-D scores#
Total	100.0	13.8	4.1 ± 2.7	
Age (year)				
65-69	32.8	10.2	3.8[a] ± 2.7	P <= 0.001[#1]
70-74	25.2	13.9	4.2 ± 3.0	
75-79	19.5	15.9	4.3[b] ± 2.9	
80-84	13.9	19.3	4.4[c] ± 2.2	
85+	8.7	15.9	4.4[d] ± 2.1	
Gender				
Women	55.0	16.0	4.2 ± 2.8	P = 0.006
Men	45.0	11.1	4.0 ± 2.5	
Sleep duration (h)				
< 6	10.7	21.2	4.7[a] ± 3.4	P < 0.001[#2]
≥ 6 to 7	19.7	13.1	4.0[b] ± 5.0	
≥ 7 to 8	23.9	10.7	3.8[c] ± 2.5	
≥ 8 to 9	29.8	12.0	3.9[d] ± 2.5	
≥ 9	15.9	18.0	4.5[e] ± 2.7	
Educational history				
Junior high school	55.4	15.9	4.3 ± 2.6	P < 0.001
More than high school	44.6	11.3	3.9 ± 2.8	
Place of residence				
Urban	68.0	13.9	4.2 ± 2.4	P = 0.037
Rural	32.0	13.8	4.0 ± 2.8	
Sleep disturbance				
Any ins: Yes	27.8	21.0	4.8 ± 3.2	P < 0.001
No	72.2	10.7	3.8 ± 2.4	
DIS: Yes	11.1	34.8	6.0 ± 3.7	P < 0.001
No	88.9	11.2	3.9 ± 2.4	
EMA: Yes	11.5	29.1	5.7 ± 3.6	P < 0.001
No	88.5	11.9	3.9 ± 2.5	
DMS: Yes	22.9	20.2	4.8 ± 3.2	P < 0.001
No	77.1	11.9	3.9 ± 2.5	
EDS: Yes	8.1	28.1	5.2 ± 3.9	P < 0.001
No	91.9	12.6	4.0 ± 2.5	
DFL: Yes	3.7	24.4	5.3 ± 3.5	P < 0.001
No	96.3	13.4	4.0 ± 2.6	
Subjective sleep sufficiency				
Insufficient	16.8	23.3	5.0 ± 3.2	P < 0.001
Sufficient	83.2	11.7	3.9 ± 2.5	
Psychological stress				
Yes	25.1	32.9	5.7 ± 3.5	P < 0.001
No	74.9	7.4	3.6 ± 2.1	
Self-rated health				
Good	31.9	5.6	3.3[a] ± 2.1	P < 0.001[#3]
Fair	40.3	10.1	3.9[b] ± 2.3	
Poor	27.8	32.5	5.7[c] ± 3.3	
Activity of daily living (ADL)				
Any	12.7	35.9	6.0 ± 3.3	P < 0.001
None	87.3	11.8	3.9 ± 2.5	

*Calculation of prevalence (%) was conducted by 11-item Short Forms of CES-D (cut-off point = 7). #Comparisons of 2 categories were performed with unpaired Student *t*-test; and comparison of ≥ 3 categories were performed with one way ANOVA and Tukey method of multiple comparison #1Statistically significant pairs among the age groups were [a] and [b], [a] and [c], [a] and [d], [a] and [e]. #2Statistically significant pairs among the sleep durations were [a] and [b], [a] and [c], [d] and [e], [c] and [e]. #3Statistically significant pairs among the categories of self-rated health were [a] and [b], [a] and [c], [b] and [c]. Any ins refers to any of DIS, EMA or DMS; DIS, difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep; EDS, excessive daily sleepiness; DFL, discomfort feeling in the legs.

Table 4—Association between depression and ANY insomnia subtypes by univariate and multivariate analyses in the cross-sectional study and longitudinal study[a]

	Univariate logistic regression analysis					
Baseline items in 2003	**Cross-sectional study in 2003**			**Longitudinal study from 2003 to 2006**		
Category	**OR[b]**	**95% CI**	**P-value**	**OR[b]**	**95% CI**	**P-value**
Sleep disturbance						
ANY ins: Yes	2.217	1.832 to 2.682	< 0.001	1.460	1.111 to 1.918	0.007
No	1.000	referent		1.000	referent	
	Multivariate logistic regression analysis					
Baseline items in 2003	**Cross-sectional study in 2003**			**Longitudinal study from 2003 to 2006**		
Category	**aOR[c]**	**95% CI**	**P-value**	**aOR[c]**	**95% CI**	**P-value**
Age (y)						
65-69	1.000	referent		1.000	referent	
70-74	1.358	1.005 to 1.836	0.046	1.252	0.894 to 1.753	0.191
75-79	1.626	1.183 to 2.235	0.003	1.020	0.688 to 1.511	0.922
80-84	2.008	1.399 to 2.883	0.000	1.394	0.876 to 2.218	0.161
85+	1.609	0.959 to 2.700	0.072	1.384	0.654 to 2.928	0.396
Gender						
Women	1.361	1.076 to 1.722	< 0.001	1.298	0.979 to 1.720	0.070
Men	1.000	referent		1.000	referent	
Educational history						
Junior high school	0.864	0.742 to 1.005	0.059	0.924	0.777 to 1.098	0.368
More than high school	1.000	referent		1.000	referent	
Place of residence						
Urban	1.073	0.804 to 1.374	0.577	1.000	0.743 to 1.346	0.999
Rural	1.000	referent		1.000	referent	
Sleep duration (h)						
< 6	1.337	0.905 to 1.973	0.144	0.875	0.508 to 1.505	0.629
≥ 6 to 7	1.015	0.722 to 1.428	0.932	1.259	0.851 to 1.865	0.249
≥ 7 to 8	1.000	referent		1.000	referent	
≥ 8 to 9	1.083	0.783 to 1.497	0.631	1.218	0.842 to 1.764	0.295
≥ 9	1.289	0.884 to 1.877	0.187	1.126	0.693 to 1.828	0.632
Sleep disturbance						
ANY ins: Yes	1.272	1.000 to 1.618	< 0.001	1.293	0.959 to 1.744	0.092
No	1.000	referent		1.000	referent	
EDS: Yes	1.418	1.008 to 1.995	0.045	0.850	0.497 to 1.453	0.551
No	1.000	referent		1.000	referent	
DFL: Yes	0.853	0.506 to 1.439	0.551	1.096	0.494 to 2.429	0.822
No	1.000	referent				
Subjective sleep sufficiency						
Insufficient	1.867	1.426 to 2.444	< 0.001	1.045	0.711 to 1.536	0.822
Sufficient	1.000	referent		1.000	referent	
Psychological stress						
Yes	5.357	4.246 to 6.758	< 0.001	1.633	1.187 to 2.246	0.003
No	1.000	referent		1.000	referent	
Self-rated health						
Good	0.671	0.491 to 0.918	0.013	0.824	0.597 to 1.137	0.239
Fair	1.000	referent		1.000	referent	
Poor	2.917	2.254 to 3.774	< 0.001	2.533	1.793 to 3.579	< 0.001
Activity of daily living (ADL)						
Any	1.496	1.053 to 2.124	0.024	1.251	0.691 to 2.262	0.460
None	1.000	referent		1.000	referent	

[a]The cross-sectional study was conducted on baseline subjects in 2003; the longitudinal study was conducted on subjects who participated in both the 2003 and 2006 surveys. [b]Crude odds ratio due to univariate logistic regression analysis. [c]Adjusted odds ratio due to multivariate logistic regression analysis. ANY ins refers to any of difficulty initiating sleep, early morning awakening, or difficulty maintaining sleep; EDS, excessive daytime sleepiness; DFL, discomfort feeling in the legs; 95%CI, 95% confidence interval.

DISCUSSION

An important feature of this study is that it was designed longitudinally so that the relationship between insomnia symptoms and depression could be examined in temporal order. A second feature is that we differentiated among the diverse components of insomnia, namely, DIS, EMA, and DMS. The study indicated that DIS had a statistically significant relationship to developing depression three years later, while EMA and DMS did not. As far as we know, there have been no reports, based on longitudinal studies of elderly Japanese, on this relationship. Our findings thus provide an important reference point for further studies on the association between insomnia subtypes and depression.

A sizable literature supports insomnia as a risk factor for depression. Yet, insomnia is a composite pathological entity consisting of such various symptoms as DIS, EMA, and DMS, and it has not been established which of these contribute to the development of depression. On the basis of the survey results on the Japanese general population in 2000, Kaneita et al.[2] reported that DIS, EMA, and DMS were related independently to depression. Although their investigation enabled us to understand the significance and separate correlation between these symptoms and depression, because of the cross-sectional nature of the data, their study could not assess the direction of effect between each symptom and the presence of depression. Our current study takes us one step further towards understanding the relationship between the presence of depression and subtypes of insomnia.

Previous studies on depression using cross-sectional data have attached more importance to EMA than DIS.[3,35] Although in our own univariate and multivariate cross-sectional analyses a significant relationship was found between EMA and the presence of depression, no statistically significant relationship between them was found in our multivariate longitudinal analysis. In the present investigation we adjusted for these associated phenomena by employing multivariate analysis; otherwise it might have been possible

for EMA to present a seemingly high correlation. To elucidate the relationship between insomnia symptoms and depression, it appears essential to design longitudinal studies with due attention to the adjustment of associative factors. As a result, we found a statistically significant relationship between DIS and the presence of depression, but not between EMA and depression. In addition, we found a statistically and substantively significant effect of psychological stress and poor self-rated health on the presence of depression. These relationships may need to be studied further using longitudinal data.

Our findings, moreover, may shed light on the bidirectional relationship between insomnia and depression. Buysse et al.,[13] using a longitudinal cohort study of young adults, expressed the bidirectional relationship between insomnia and depression in temporal order without specifying particular insomnia subtypes. They stated that "insomnia predicted future MDE (major depressive episodes) and that MDE tended to predict future insomnia." Based on our study, DIS seems to precede the presence of depression. Rodin et al.[17] followed 196 subjects aged 62 and over for three years and indicated that depression is related to sleep disturbance, particularly EMA. EMA possibly arose as a result of depression. If one were to examine, using longitudinal data, the relationship between depression and insomnia as a composite measure that includes DIS and EMA, one might find a bidirectional relationship between depression and insomnia. If this relationship between DIS, depression, and EMA holds in the cross-sectional studies, we should observe the significant association both between DIS and depression, and depression and EMA, as observed in the present study. However, the results from the cross-sectional studies may be misleading. In the future, we plan to study the relationship between the presence of depression and EMA in the opposite direction, as examined by Rodin et al.[17]

Although our study produced different results from those of previous studies, it is quite difficult to compare

Table 5—Association between depression and insomnia subtypes in the cross-sectional study[a]

	Logistic regression analyses					
Baseline items in 2003	**Univariate analysis**			**Multivariate analysis**		
Category	**OR[b]**	**95% CI**	**P-value**	**aOR[c]**	**95% CI**	**P-value**
Age (year)						
65-69	1.000	referent		1.000	referent	
70-74	1.423	1.101 to 1.838	0.006	1.359	1.001 to 1.844	0.049
75-79	1.675	1.282 to 2.189	< 0.001	1.620	1.174 to 2.235	0.003
80-84	2.121	1.584 to 2.841	< 0.001	1.986	1.375 to 2.867	< 0.001
85+	1.673	1.117 to 2.508	0.013	1.516	0.889 to 2.583	0.126
Gender						
Women	1.526	1.257 to 1.853	< 0.001	1.327	1.047 to 1.681	0.019
Men	1.000	referent		1.000	referent	
Educational history						
Junior high school	0.669	0.552 to 0.811	< 0.001	0.790	0.622 to 1.004	0.054
More than high school	1.000	referent		1.000	referent	
Place of residence						
Urban	0.987	0.807 to 1.208	0.898	1.066	0.830 to 1.370	0.616
Rural	1.000	referent		1.000	referent	
Sleep duration (h)						
< 6	2.238	1.628 to 3.075	< 0.001	1.162	0.776 to 1.742	0.466
≥ 6 to 7	1.261	0.939 to 1.693	0.124	0.944	0.667 to 1.337	0.747
≥ 7 to 8	1.000			1.000	referent	
≥ 8 to 9	1.132	0.858 to 1.495	0.380	1.098	0.792 to 1.521	0.575
≥ 9	1.823	1.337 to 2.487	<0.001	1.349	0.923 to 1.972	0.122
Sleep disturbance						
DIS: Yes	4.208	3.329 to 5.319	< 0.001	2.020	1.455 to 2.805	< 0.001
No	1.000	referent		1.000	referent	
EMA: Yes	3.049	2.403 to 3.870	< 0.001	1.441	1.025 to 2.026	0.036
No	1.000	referent		1.000	referent	
DMS: Yes	1.869	1.525 to 2.289	< 0.001	0.819	0.613 to 1.094	0.176
No	1.000	referent		1.000	referent	
EDS: Yes	2.716	2.064 to 3.574	< 0.001	1.319	0.929 to 1.875	0.122
No	1.000	referent		1.000	referent	
DFL: Yes	2.131	1.465 to 3.101	< 0.001	0.788	0.463 to 1.342	0.381
No	1.000	referent		1.000	referent	
Subjective sleep sufficiency						
Insufficient	2.290	1.839 to 2.852	< 0.001	1.758	1.335 to 2.315	< 0.001
Sufficient	1.000	referent		1.000	referent	
Psychological stress						
Yes	6.104	4.997 to 7.455	< 0.001	5.169	4.088 to 6.537	< 0.001
No	1.000	referent		1.000	referent	
Self-rated health						
Good	0.531	0.397 to 0.709	< 0.001	0.664	0.485 to 0.910	0.011
Fair	1.000	referent		1.000	referent	
Poor	4.270	3.435 to 5.307	< 0.001	2.187	3.688 to 3.231	< 0.001
Activities of daily living (ADL)						
Any	4.180	3.211 to 5.443	< 0.001	1.419	0.991 to 2.032	0.056
None	1.000	referent		1.000	referent	

[a]The cross-sectional study was conducted on baseline subjects in 2003. [b]Crude odds ratio due to univariate logistic regression analysis. [c]Adjusted odds ratio due to multivariate logistic regression analysis. The logistic regression analysis was conducted as a response variable of CES-D (Score ≥ 7) by the short form. DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep; EDS, Exceesive daytime sleepiness; DFL, discomfort feeling in the legs; 95%CI, 95% confidence interval.

Table 6—Association between depression and insomnia subtypes in the longitudinal study (2003-2006)[a] for subjects without depression in 2003

Baseline items in 2003	Logistic regression analyses					
	Univariate analysis			Multivariate analysis		
Category	OR[b]	95% CI	P-value	aOR[c]	95% CI	P-value
Age (y)						
65-69	1.000	referent		1.000	referent	
70-74	1.333	0.966 to 1.840	0.081	1.219	0.869 to 1.711	0.252
75-79	1.144	0.788 to 1.660	0.480	1.006	0.677 to 1.493	0.978
80-84	1.728	1.131 to 2.640	0.012	1.347	0.841 to 2.157	0.215
85+	1.657	0.851 to 3.224	0.137	1.344	0.634 to 2.849	0.441
Gender						
Women	1.253	0.966 to 1.627	0.090	1.327	1.000 to 1.761	0.050
Men	1.000	referent		1.000	referent	
Educational history						
Junior high school	0.874	0.675 to 1.131	0.306	0.906	0.680 to 1.206	0.499
More than high school	1.000	referent		1.000	referent	
Place of residence						
Urban	0.948	0.721 to 1.246	0.700	0.968	0.718 to 1.305	0.832
Rural	1.000	referent		1.000	referent	
Sleep duration (h)						
< 6	1.147	0.694 to 1.894	0.593	0.849	0.487 to 1.481	0.564
≥ 6 to 7	1.378	0.948 to 2.004	0.093	1.227	0.824 to 1.828	0.314
≥ 7 to 8	1.000	referent		1.000	referent	
≥ 8 to 9	1.246	0.878 to 1.770	0.219	1.218	0.839 to 1.767	0.300
≥ 9	1.319	0.840 to 2.073	0.229	1.175	0.722 to 1.912	0.517
Sleep disturbances						
DIS: Yes	2.042	1.391 to 2.997	< 0.001	1.592	1.012 to 2.504	0.044
No	1.000	referent		1.000	referent	
EMA: Yes	1.541	1.030 to 2.306	0.035	1.070	0.664 to 1.723	0.782
No	1.000	referent		1.000	referent	
DMS: Yes	1.432	1.066 to 1.925	0.017	1.215	0.860 to 1.716	0.269
No	1.000	referent		1.000	referent	
EDS: Yes	1.401	0.869 to 2.260	0.166	0.819	0.477 to 1.408	0.471
No	1.000	referent		1.000	referent	
DFL: Yes	2.120	1.125 to 3.995	0.020	0.990	0.440 to 2.230	0.981
No	1.000	referent		1.000	referent	
Subjective sleep sufficiency						
Insufficient	1.093	0.760 to 1.573	0.631	1.051	0.713 to 1.547	0.803
Sufficient	1.000	referent		1.000	referent	
Psychological stress						
Yes	1.846	1.375 to 2.479	< 0.001	1.553	1.125 to 2.145	0.008
No	1.000	referent		1.000	referent	
Self-rated health						
Good	0.745	0.546 to 1.016	0.063	0.794	0.574 to 1.099	0.164
Fair	1.000	referent		1.000	referent	
Poor	2.589	1.881 to 3.563	< 0.001	2.517	1.778 to 3.562	< 0.001
Activity of daily living (ADL)						
Any	2.223	1.312 to 3.766	0.003	1.207	0.664 to 2.193	0.538
None	1.000	referent		1.000	referent	

[a]The longitudinal study was conducted on subjects participating in the 2003 and 2006 surveys, with the former serving as the baseline. [b]Crude odds ratio due to univariate logistic regression analysis. [c]Adjusted odds ratio due to multivariate logistic regression analysis, the logistic regression analysis was conducted as a response variable of CES-D (score ≥ 7) by Shorter Form in 2006.
DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep; EDS, excessive daytime sleepiness; DFL, discomfort feeling in the legs; 95%CI, 95% confidence interval.

studies on the relationship between insomnia and depression because the definition, criteria, and measures of insomnia and depression were different for each study. One plausible reason why we had different results is that our criteria for insomnia symptoms were less strict and, therefore, individuals with transient and minor sleep disturbances may have been included. More specifically, it may have caused a relative increase in sleep maintenance complaints among the elderly population. As a result, minor transient insomniacs may have diluted the clinical sample of sleep maintenance insomniacs, possibly reducing the specificity of this particular symptom for predicting later presence of depression.

Insomnia, which is defined rather loosely in our study, could be another concern for our longitudinal study. As mentioned before, questions on insomnia subtypes used in the study relied on self-reports without reference to time. Our findings were not particularly robust, and odds ratios in our results were relatively low compared to ones found in previous longitudinal studies. In order to examine the effect of changes in definitions of insomnia, we have run another model for a longitudinal study with more strict criteria for insomnia subtypes. We defined presence of insomnia subtypes only for those who answered "always" (we included both "often" and "always" in our present study because of obtaining stable estimates). Adjusted odds ratios (95% CI) for DIS increased from 1.592 (1.012 to 2.504) to 2.086 (1.091 to 3.989) with a significance level of 0.026. This indicates that to examine the relationship between DIS and depression in the longitudinal study may be warranted. In any case, given that epidemiological data on the relationship between insomnia subtypes and the development of depression are relatively scarce, it is hoped that many more longitudinal studies on this subject will be carried out and more knowledge accumulated.

Study Limitations

This study has a few limitations. First, our study participants were limited to those aged 65 and older.

Studies with the general population should be conducted to see whether our conclusions apply to the population at large.

Second, we evaluated depression using only the CES-D scale. Neither the DSM-IV[4] nor the ICD-10[36] are applicable to a community-based survey, and, therefore, could not be employed to diagnose clinically the subjects of our study. Many epidemiological studies have, in fact, relied on the CES-D scale, as its reliability and validity have been sufficiently established. Nevertheless, given that comparing disease prevalence among regions is problematic[37] and that clinical diagnoses and CES-D scale evaluations of depression do not always agree,[38] the use of other diagnostic methods should be considered in the future.

Third, because at the time of the baseline survey we did not ask participants whether they had ever had depression before, we may be examining the relationship between insomnia subtypes and recurrence of depression rather than between insomnia subtypes and initial onset of depression.

Fourth, as is commonly found in epidemiological work, we did not have objective data on disturbed sleep. While it is desirable to obtain objective data, it is very difficult to conduct such studies on a community scale. More objective and yet simple epidemiological research techniques should be developed. In addition, we did not make an insomnia diagnosis using established criteria. We simply used endorsement of specific insomnia subtypes which did not include a time frame or frequency. Moreover, because of the data limitation, we did not utilize daytime impairment/dysfunction as required by most current insomnia nosologies.

Fifth, the association between insomnia symptoms and the presence of depression was evaluated only at two points in the three-year period. No specific information on depression was obtained regarding when during the three years the condition developed, nor how long the condition lasted. In addition, three years may be too long to observe the association between insomnia symptoms and depression. Although, as in the present study, several longitudinal studies on sleep disorder have evaluated results using information from two study points, the number of observation points chosen and the duration of the study should receive careful consideration in future studies.

Lastly, we should point out the possibility of non-response bias in our study. Because a longitudinal study is destined to lose participants by death and lost-to-follow-up, only those who have managed to maintain health tend to be surveyed in the follow-up. In addition, proxy responses and non response to CES-D questions tend to increase as participants age. In order for the study of precursor symptoms and risk factors of insomnia to be meaningful, due attention in future studies should be given to the upper age limit in studies.

Despite these limitations, we hope that our study results will contribute to the future progress of mental health care and the solution of sleeping problems. If our findings are found to be true by clinical research, DIS subtype is possibly a better predictor of depression than overall insomnia severity. By understanding better the relationship between depression and insomnia subtypes, we may have a chance to lower the prevalence of depression among older adults in Japan.

Table 7—Comparison of adjusted odds ratios (95% CI) of 10-item CES-D scale and 11-item CES-D scale based on multivariate analyses of the association of insomnia subtypes with depression in cross-sectional and longitudinal study

	10-item CES-D Scale				11-item CES-D Scale*	
	Cut-off point = 6		Cut-off point = 7		Cut-off point = 7	
Insomnia Subtypes	Cross-sectional study					
	aOR#	95%CI	aOR	95%CI	aOR	95%CI
DIS	1.819	(1.327 to 2.493)	1.721	(1.214 to 2.439)	2.020	(1.455 to 2.805)
EMA	1.262	(0.910 to 1.748)	1.476	(1.030 to 2.114)	1.441	(1.025 to 2.026)
DMS	0.874	(0.669 to 1.142)	0.899	(0.662 to 1220)	0.819	(0.613 to 1.094)
	Longitudinal study					
	aOR	95%CI	aOR	95%CI	aOR	95%CI
DIS	1.659	(1.047 to 2.629)	1.444	(0.936 to 2.227)	1.592	(1.012 to 2.504)
EMA	1.242	(0.773 to 1.993)	1.153	(0.735 to 1.808)	1.070	(0.664 to 1.723)
DMS	1.304	(0.916 to 1.854)	1.263	(0.905 To 1.763)	1.215	(0.860 to 1.716)

*Results were taken from Table 5 for the cross-sectional study and from Table 6 for the longitudinal study. #aOR: adjusted odds ratio and 95%CI; 95% confidence interval. Logistic regression analysis was conducted by controlling for age, gender, educational history, place of residence, sleep duration, excessive day time sleepiness, discomfort feeling in the legs, subjective sleep sufficiency, psychological stress, self-rated health, and activities of daily living. DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep.

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REFERENCES

1. Murray CJL, Lopez AD, eds. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge, MA, Harvard School of Public Health on behalf of World Health Organization and the World Bank, 1996 (Global Burden of Disease and Injury Series, Vol. I).
2. Kaneita Y, Ohida T, Uchiyama M, et al. The relationship between depression and sleep disturbances: a Japanese nationwide general population survey. J Clin Psychiatry 2006; 67:196-203.
3. Lustberg L, Reynolds CF. Depression and insomnia: questions of cause and effect. Sleep Med Rev 2000;4:253-62.

4. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: American Psychiatric Association, 1994.
5. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989;262:1479-84.
6. Breslau N, Roth T, Rosenthal L, et al. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adult. Biol Psychiatry 1996;39:411-8.
7. Chang PP, Ford DE, Mead LA, et al. Insomnia in young men and subsequent depression: the Johns Hopkins precursors study. Am J Epidemiol 1997;146:105-14.
8. Riemann D, Voderholzer U. Primary insomnia: a risk factor to develop depression? J Affect Disord 2003;76:255-9.
9. Brabbins CJ, Dewey ME, Copeland RM, et al. Insomnia in the elderly: prevalence, gender differences and relationship with morbidity and mortality. Int J Geriatr Psychiatry 1993;8:473-80.
10. Foley DJ, Monjan A, Simonsick EM, et al. Incidence and remission of insomnia among elderly adults: an epidemiological study of 6800 persons over 3 years. Sleep 1999;22(Suppl2):366-72.
11. Morphy H, Dunn KM, Lewis M, Boardman HF, Croft PR. Epidemiology of insomnia: a longitudinal study in a UK population. Sleep 2007;30:274-80.
12. Neckelmann D, Mykletun A, Dahl AA. Chronic Insomnia as a risk factor for developing anxiety and depression. Sleep 2007;30:873-80.
13. Buysse DJ, Angst JA, Gamma A, et al. Prevalence, course, and comorbidity of insomnia and depression in young adults. Sleep 2008; 31:473-80.
14. Jansson-Frojmark M, Lindblom K. A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. J Psychosom Res 2008; 64:443-9.
15. Kim JM, Stewart R, Kim SW, et al. Insomnia, depression, and physical disorders in late life: a 2-year longitudinal community study in Korea. Sleep 2009;32:1221-8.
16. Hartz AJ, Daly JM, Kohatsu ND, et al. Risk factors for insomnia in a rural population. Ann Epidemiol 2007;17: 940-7.
17. Rodin J, McAvay G, Timko C. A longitudinal study of depressed mood and sleep disturbances in elderly adults. J Gerontol 1988;43:45-53.
18. Sukegawa T, Itoga M, Seno H, et al. Sleep disturbance and depression in the elderly in Japan. Psychiatry Clin Neurosci 2003; 57:265-70.
19. Saito Y. A survey on health and lifestyle. Report series No.1. The Nihon University Center for Information Networking 2000. (in Japanese)
20. Kohout FJ, Berkman LF, Evans DA, Huntley JC. Two shorter forms of the CES-D depression symptom index. J Aging Health 1993;5:179-93.
21. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385-401.
22. Shima S, Shikano T, Kitamura T, Asai M. New self-rating scales for depression. SEISHIN IGAKU 1985; 27:717-723. (in Japanese)
23. Yokoyama E, Kaneita Y, Saito Y, et al. Cut-off point for the 11-item shorter form of the CES-D Depression Scale. Nihon Univ. J Med 2008;50:123-32.
24. Kim K,Uchiyama M,Okawa M,Liu X, Ogihara R. An epidemiological study of insomnia among the Japanese general population. Sleep 2000;23:41-7.
25. Liu X, Uchiyama M, Kim K, et al. Sleep loss and daytime sleepiness in the general adult population of Japan. Psychiatr Res 2000;93:1-11.
26. Ohida T, Osaki Y, Doi Y, et al. An epidemiologic study of self-reported sleep problems among Japanese adolescents. Sleep 2004;27:975-85.
27. Kaneita Y, Ohida T, Uchiyama M, et al. Excessive daytime sleepiness among Japanese general population. J Epidemiol 2005;15:1-8.
28. Suzuki K, Ohida T, Sone T, et al. The prevalence of restless legs syndrome among pregnant women in Japan and the relationship between restless legs syndrome and sleep problems. Sleep 2003; 26:673-7.
29. Ekbom KA. Restless legs. Acta Med Scand 1945; 158 (Suppl):4-122.
30 Roberts RE, Kaplan GA, Shema SJ, et al. Prevalence and correlates of depression in an aging cohort: the Alameda county study. J Gerontol B Psychol Sci Soc Sci 1997; 52B:S252-8.
31. Livingston G, Blizard B, Mann A. Does sleep disturbance predict depression in elderly people? A study in inner London. Br J Gen Pract 1993;43:445-8.
32. Roberts RE, Shema SJ, Kaplan GA, Strawbridge WJ. Sleep complaints and depression in an aging cohort: A prospective perspective. Am J Psychiatry 2000;157:81-88.
33. Idler EL, Benyamini Y. Self-rated health and mortality. A review of twenty-seven community studies. J Health Soc Behav 1997; 38: 21-37.
34. SAS Institute Inc. SAS User's Guide: Statistics, Version 9.1. 2004. Cary, NC. USA.
35. Reynolds CF, Hoch CC, Kuper DJ et al. Bedside differentiation of depression pseudodementia from dementia. Am J Psychiatry 1988;145:1099-103.
36. World Health Organization. International Classification of Disease and Related Health Problems 10th Revision, 1992.
37. Mackinnon A, MaCallum J, Anderson I. The Center for Epidemiological Studies Depression Scale in older samples in Indonesia, North Korea, Myanmar, Sri Lanka, and Thailand. J Gerontol B Psychol Sci Soc Sci 1998;53:343-52.
38. Katona C, Livingstone G. Impact of screening of old people with physical illness for depression? Lancet 2000;356:91-2.

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Sleep-related problems and use of hypnotics in inpatients of acute hospital wards

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Abstract

Objective: Although sleep disorders are highly prevalent among patients with physical disorders, only limited information is available about the actual status of sleep-related problems in inpatients of acute hospital wards. We conducted a multicenter cross-sectional observational survey investigating the prevalence of sleep disorders and use of hypnotic-sedative drugs among inpatients of acute wards in 44 general hospitals in Japan.

Method: Questionnaire-, actigraph- and observation-based sleep evaluations were simultaneously performed in 557 adult inpatients [mean age 72.8±12.8 (S.D.) years] of acute wards during a one-month period in July 2007.

Results: Of the 421 patients with data available, 22.3% had at least one of the following sleep disorders: sleep apnea syndrome, restless legs syndrome, periodic limb movement disorder and nocturnal behavior disorder. Similarly, 62.7% had insomnia, 6.9% had severe daytime sleepiness and 12.8% had other sleep-related symptoms. Only 13.8% were free of any sleep-related problem. Although 33.7% of insomnia patients were taking hypnotic-sedative drugs, 65.2% of them complained of residual insomnia symptoms.

Conclusion: The findings obtained in this study have revealed the remarkably high prevalence of sleep-related problems experienced by inpatients of acute hospital wards in Japan. Proper diagnosis of sleep disorders should be made among patients with physical disorders.

Keywords: Sleep disorders; Insomnia; Acute hospital wards; Physical illness; Hypnotic use

1. Introduction

Sleep disorders, including insomnia, sleep apnea syndrome (SAS), restless legs syndrome (RLS) and periodic limb movement disorder (PLMD), are highly prevalent and particularly common in elderly patients with physical disorders. Sleep disorders reduce patients' quality of life (QOL) by causing symptoms such as daytime sleepiness and cognitive impairment and may also exacerbate underlying disorders by inhibiting respiratory, cardiovascular and

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metabolic functions. In one study of older patients in a skilled-care geriatric hospital in Japan, the presence of insomnia was associated with a higher risk of mortality during the 2-year follow-up period [1].

The prevalence of these sleep disorders increases with age [2], and the high incidence of physical disorders among the elderly population is a contributing factor. Previous epidemiologic studies have revealed that the prevalence of insomnia among the general population is 10.2–48.0% [3–6], and insomnia frequently occurs in association with chronic pain disorders, respiratory diseases and neurological diseases [7]. SAS, RLS or PLMD also frequently coexists with various physical diseases including hypertension [8], ischemic heart disease [9,10], chronic kidney failure [11], iron-deficiency anemia [12] and neurological diseases such as Parkinson's disease [13]. It is also noteworthy that medications used for the treatment of sleep disorders may worsen physical disorders; for example, most standard hypnotics benzodiazepines cause *sleep apnea* by reducing the muscle tone of the upper respiratory tract during sleep [14].

The fact that physical and sleep disorders can coexist at a high frequency should always be taken into account when making an accurate diagnosis and developing a treatment strategy that provides a favorable risk-benefit balance. Nevertheless, we currently have only limited information about the actual status of sleep-related problems experienced by inpatients of acute hospital wards. Thus, the objectives of the present study were to investigate the breakdown and prevalence of sleep disorders and use of hypnotic-sedative drugs in acute ward inpatients and to identify problems in the clinical practice of sleep medicine.

2. Methods

2.1. Subjects and method

Study subjects who were 20 years of age or more were randomly selected from among the inpatients of acute hospital wards, excluding psychiatric and tuberculosis wards, of 44 general hospitals in Japan. The patients' identities were coded at each hospital ward, and then patients were randomly sampled. The investigation was carried out among 557 subjects [316 males, 241 females; mean age, 72.8±12.8 (S.D.) years; range 22–96 years] who had provided informed consent or whose family member had provided informed consent, simultaneously at all hospitals during a period of 1 month in July 2007. Each patient's primary disorder was classified according to the International Classification of Diseases and Related Health Problems Version 10 (*ICD-10*) (Table 1). The ethics committee at each research site approved the present study.

2.2. Investigation methods

The investigation was conducted over 2 days for each patient to check his or her sleep condition and details of treatment. The investigation consisted of subjective sleep evaluation using a self-administered questionnaire (Table 2), objective sleep evaluation by actigraphy, observational sleep evaluation by nursing staff and a survey of medication use as recorded in the medical records.

The questionnaire was designed to identify the presence of insomnia, SAS, RLS, PLMD, nocturnal behavior disorder (NBD), daytime sleepiness and nocturnal sleep-related symptoms. In the questionnaire, Q1–Q6 were completed by the patients, and Q7 and Q8 were completed by medical staff. Although NBD can be further divided into nocturnal delirium, REM sleep behavior disorder, behavioral and psychological symptoms of dementia and other symptoms, these disorders were not distinguished in view of the primary objective of the present study and technical restrictions.

For objective sleep evaluation, subjects were asked to wear an actigraph [Lifecorder PLUS (LC), Suzuken, Nagoya, Japan] [15] on their waist for two consecutive days for continuous recording of the intensity of activity. Total sleep time (TST; the sum of all sleep time during time in bed), total wake time (TWT; the sum of all wake time during time in bed) and sleep efficiency (SE; the percentage of TST relative to time in bed) were then calculated from the LC data. Time in bed (TIB) was defined as the time during

Table 1
Illness identified in enrolled patients

System organ/disease class	Total	SAS, RLS, PLMD and NBD	Insomnia			Good Sleep
	557 (100%)	94 (100%)	Improved 31 (100%)	Untreated 175 (100%)	Not-Improved 58 (100%)	63 (100%)
Diseases of the circulatory system	140 (25.1)	20 (21.3)	7 (22.6)	44 (25.1)	9 (15.5)	15 (23.8)
Neoplasms	127 (22.8)	19 (20.2)	5 (16.1)	47 (26.9)	26 (44.8)	8 (12.7)
Diseases of the respiratory system	68 (12.2)	11 (11.7)	3 (9.7)	17 (9.7)	8 (13.8)	9 (14.3)
Diseases of the digestive system	62 (11.1)	13 (13.8)	2 (6.5)	21 (12.0)	7 (12.1)	8 (12.7)
Diseases of the nervous system	45 (8.1)	11 (11.7)	2 (6.5)	9 (5.1)	3 (5.2)	5 (7.9)
Diseases of the genitourinary system	16 (2.9)	4 (4.3)	1 (3.2)	5 (2.9)	1 (1.7)	3 (4.9)
Diseases of the musculoskeletal system and connective tissue	14 (2.5)	2 (2.1)	1 (3.2)	7 (4.0)	0 (0.0)	3 (4.9)
Certain infectious and parasitic diseases	8 (1.4)	0 (0.0)	1 (3.2)	3 (1.7)	1 (1.7)	0 (0.0)
Other diseases	77 (13.8)	14 (14.9)	9 (29.0)	22 (12.6)	3 (5.2)	12 (19.0)

SAS; sleep apnea syndrome, RLS; restless legs syndrome, PLMD; periodic limb movement disorder, NBD; nocturnal behavior disorder.

Table 2
Question items and percentages of respondents in the analyzed 421 inpatients

Items		1)	2)	3)	4)
Q1. How long did it take from light off until you went to sleep?					
1) less than 15 minutes 2) 15-29 minutes 3) 30-59 minutes 4) more than 60 minutes		50.4	20.4	14.5	14.7
Q2. How many times did you awake during last night?					
1) none 2) 1-2 times 3) 3-4 times 4) more than 5 times		21.4	35.9	24.9	17.8
Q3. What time did you get up this morning (h:min)?		22.6*	77.4		
Q4. Did you get up in the morning unrefreshed or nonrestored?					
1) good 2) fair 3) insufficient 4) poor		38.7	37.1	19.2	5.0
Q5. Do you have daytime sleepiness?**					
1) none 2)some 3) moderate 4) severe		22.8	22.8	47.5	6.9
Q6. Did you experience any of the following symptoms during last night (completed by a patient)					
Q6-a creeping sensation or restless discomfort in the limbs	1) yes 2) no	5.9	94.1		
Q6-b legs or arms jerk	1) yes 2) no	2.4	97.6		
Q6-c hot flash	1) yes 2) no	4.8	95.2		
Q6-d night sweat	1) yes 2) no	6.9	93.1		
Q6-e palpitation	1) yes 2) no	1.2	98.8		
Q6-f anxiety or panic	1) yes 2) no	1.0	99.0		
Q6-g sleep paralysis	1) yes 2) no	0.0	100.0		
Q6-h nightmare	1) yes 2) no	3.1	96.9		
Q7. Did the patient experience any of the following symptoms during last night (completed by nursing staffs)					
Q7-a loud snoring, or apnea lasting for 10 seconds or longer	1) yes 2) no	10.0	90.0		
Q7-b periodic legs or arms jerk	1) yes 2) no	2.1	97.9		
Q7-c sleep-talking, delirium or abnormal behaviors such as wandering	1) yes 2) no	6.9	93.1		
Q8. Whether or not the patient took any hypnotic-sedative drug(s) for treatment of insomnia within the past one week and the name of the drug(s) if any (completed by nursing staffs)					
1) yes 2) no Name of drugs [ ]		27.6	72.4		

* Patients who woke up 30 minutes or earlier than the desired time without falling asleep again (Q3).
** answered at 2 pm.

which patients were supposed to be in bed as specified by each hospital ward, and specifically the time from "lights out" to the time at which patients were expected to wake. Mean TIB was approximately between 9 p.m. and 6 a.m. Observations by the nursing staffs on each of the wards confirmed that the patients were in bed during TIB on the evenings of the study.

For the observational sleep evaluations, several nursing staffs alternated in order to record continuously the subjects' sleep states. Opening and closing of eyes, breathing, movement and any unusual behavior of the subjects were observed and recorded at a distance so as to not disturb the subjects.

2.3. Differential diagnosis of sleep disorders

The diagnostic flow for the patients included in the investigation is shown in Fig. 1. Some of the preselected subjects (n=136) were either excluded from data analyses or could not participate due to reasons such as sudden change in physical condition such as fever, severe dementia, consciousness disturbance due to organic brain damages, need for emergency examination, hospital transfer or discharge or due to missing data on their amount of physical activity. As a result, a total of 421 patients comprised the analysis population [228 males, 193 females; mean age, 72.5±12.6 (S.D.) years; range 22-96 years]. The number of respondents for each question item is shown in Table 2.

Patients were initially examined for the presence of SAS (positive answer to Q7-a), RLS (positive answer to Q6-a), PLMD (positive answer to Q6-b or Q7-b) or NBD (positive answer to Q7-c). Those who were NOT diagnosed with SAS, RLS, PLMD or NBD were subsequently examined for the presence of insomnia. Patients were judged as having insomnia when the subjective sleep investigation indicated the presence of any one of the following:

i. Disturbances of initiating sleep (DIS): Q1, the answer indicates 30 min or more.
ii. Disturbances of maintaining sleep (DMS): Q2, the answer indicates three times or more.
iii. Early morning awakening (EMA): Q3, the answer indicates wake time 30 minutes or earlier than the desired time without falling asleep again.
iv. Non-restorative sleep (NRS): Q4, the answer indicates insufficient or poor sleep.

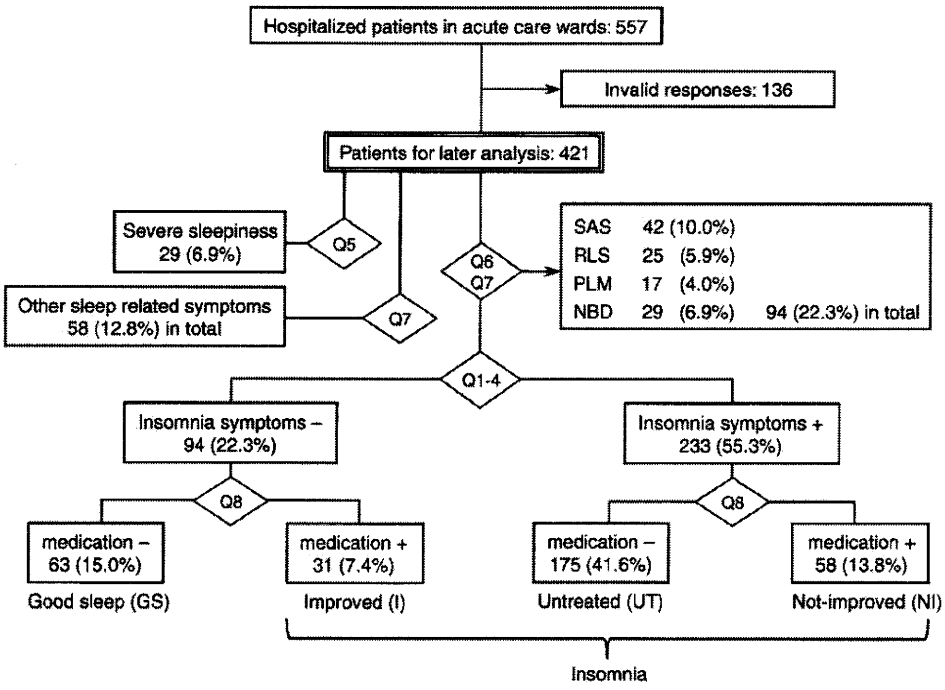

Fig. 1. Diagnostic flow of the subjects in this study. See text and Table 2 for explanation.

The subjects were also divided into the following four groups according to the presence or absence of insomnia and use or not of hypnotic-sedative drugs for insomnia treatment: the good sleep (GS) group consisting of those without insomnia and taking no medication, the improved (I) group consisting of those without insomnia and taking medication (s), the untreated (UT) group consisting of those with insomnia but taking no medication, and the not-improved (NI) group consisting of those with insomnia and taking medication(s). Of these groups, the I, UT and NI groups were grouped together and defined as the insomnia group (Fig. 1).

2.4. Daytime sleepiness

The 421 patients were examined for the presence or absence of daytime sleepiness according to the following criteria: Q5, the answer indicates the presence of moderate or severe sleepiness.

2.5. Sleep-related symptoms

The 421 patients were examined for the presence or absence of other sleep-related symptoms, such as hot flashes in the foot or body (Q6-c), night sweats (Q6-d), palpitations (Q6-e), anxiety and panic (Q6-f), sleep paralysis (Q6-g) and nightmares (Q6-h).

2.6. Statistical analysis

One-way analysis of variance followed by Tukey's multiple comparison tests was used to identify significant differences in sleep parameters (TST, TWT and SE) among the insomnia group and GS group. Sleep parameters were also compared between each sleep disorder group and the GS group using a two-tailed Student's t test. Analysis values are expressed as mean±S.D. Multiple logistic regression analysis was carried out to calculate the odds ratio (OR) and 95% confidence interval (CI) for assessing the association of primary disorders, sleep disorders and use of hypnotic-sedative drugs with severe sleepiness. Presence of severe sleepiness was used as the dependent variable, and primary disorders, sleep disorders and use of hypnotic-sedative drugs were used as independent variables. We performed multiple logistic regression analyses to control for all sociodemographic (sex and age) and other factors. Statistical significance was set at $P<.05$. All analyses were made using SPSS 11.5 for Windows.

3. Results

3.1. Prevalence of sleep disorders

The breakdown of the diagnoses of sleep disorders is shown in Fig. 1. Of the 421 inpatients, 42 (10.0%, M/F=29/13) had SAS, 25 (5.9%, 14/11) had RLS, 17 (4.0%, 11/6) had PLMD and 29 (6.9%, 19/10) had NBD. A total of 94 (22.3%) had at least one of the four sleep disorders. Seventeen patients had two sleep disorders concurrently.

Of the 421 inpatients, 58 (13.8%, NI) and 175 (41.6%, UT) complained of insomnia symptoms. A total of 264 (62.7%), including the NI, UT and I (31, 7.4%) groups were given a diagnosis of insomnia. The most common insomnia

Table 3
Comparison of objective sleep parameters determined by LC in the insomnia and good sleep patients

	SAS n=42	P	RLS n=25	P	PLMD n=17	P	NBD n=29	P	Insomnia						Good sleep n=63
									Untreated n=175	P	Improved n=31	P	Not-improved n=58	P	
TST (min)	367.6±119.2	.06	331.9±117.7	0	354.6±111.5	.01	359.8±126.1	.04	369.2±102.5	.04	400.7±118.4	n.s	399.7±91.0	n.s	409.4±102.4
TWT (min)	172.4±119.2	.05	208.1±117.7	0	185.4±111.5	.01	180.2±126.1	.04	170.3±102.3	.03	139.4±118.4	n.s	140.3±91.0	n.s	129.3±103.3
SE (%)	68.1±22.1	.05	61.5±21.8	0	65.7±20.6	.01	66.6±23.4	.04	68.4±19.0	.03	74.2±21.9	n.s	74.0±16.9	n.s	76.1±19.1

Value are expressed as mean±S.D..
P value vs. Good sleep group.
n.s; not significant.

symptom was DMS (60.1%), followed by DIS (41.2%), EMA (33.9%) and NRS (31.8%). Only 63 (15.0%) were free of the above-mentioned sleep disorders and were assigned to the GS group.

3.2. Objective sleep parameters

Sleep parameters in each sleep disorder group are summarized in Table 3. There were significant differences in TST [F(3,323)=3.24, P=.022], TWT [F(3,323)=3.28, P=.021] and SE [F(3,323)=3.31, P=.020) among the insomnia group and GS group. TST (P=.039) was significantly shorter and TWT (P=.033) and SE (P=.032) were significantly longer in the NI group than in the GS group. Patients with RLS (P<.01) and NBD (P<.05) also presented a significantly shorter TST, significantly longer TWT and significantly lower SE than those in the GS group. A similar tendency was observed for patients with SAS or PLMD (P<.06). On the other hand, we found no significant differences in the sleep parameters between the medicated group (the I or NI group) and the GS group, regardless of whether or not any subjective improvement was observed.

3.3. Daytime sleepiness

Of the 421 inpatients, 229 (54.4%) experienced moderate to severe sleepiness and 29 (6.9%) experienced severe sleepiness. Severe sleepiness was commonly observed in those with sleep disorders; it was most commonly observed in patients with multiple sleep disorders (27.8%, 5/18), followed by those with PLMD (18.2%, 2/11), SAS (17.9%, 5/28) and NBD (17.7%, 3/17). Multiple logistic regression analysis revealed that SAS (adjusted OR=3.78, 95% CI, 1.24–11.53, P<.05) and PLMD (adjusted OR=5.93, 95% CI, 1.50–23.4, P<.05) showed a significantly positive association with the presence of severe sleepiness.

3.4. Other sleep-related symptoms

Of the 421 inpatients, 19 (4.5%, M/F=7/12) had hot flashes, 29 (6.9%, 13/16) had night sweats, 5 (1.2%, 1/4) had palpitations, 4 (1.0%, 2/2) had anxiety or panic and 13 (3.1%, 7/6) had nightmares. None of the patients experienced sleep paralysis.

3.5. Prevalence of use of hypnotic-sedative drugs

Of the 421 inpatients, 116 (27.6%) were taking some kind of hypnotic-sedative drug for the treatment of insomnia symptoms. The breakdown of the prescribed drugs was as follows: benzodiazepine hypnotics including zolpidem and zopiclone accounted for 73.2% (26.1% for ultrashort-acting, 30.6% for short-acting and 16.5% for intermediate-acting), benzodiazepine anxiolytic accounted for 5.8%, antipsychotics accounted for 15.6% and other drugs accounted for 5.2% of all prescribed drugs. In the insomnia group, those receiving medication therapy for insomnia only accounted for 33.7% (the I+NI group). Two thirds of the patients receiving medication therapy (65.2%, corresponding to the NI group) complained of persistent insomnia symptoms. In addition, 36.0% of RLS patients, 29.4% of PLMD patients, 26.2% of SAS patients and 17.2% of NBD patients were taking at least one of the above hypnotic-sedative drugs.

4. Discussion

This is the first multicenter study investigating the prevalence of sleep disorders in inpatients of acute wards in general hospitals. Sleep disorders are extremely common disorders among community residents, and are even more so among patients with underlying physical diseases as in the subjects of the present study. Insomnia, as well as other sleep disorders, while frequently thought to be transitory or secondary to a physical disease, can become prolonged without appropriate treatment in the early stages. Furthermore, chronic sleep disorders can exacerbate lifestyle-related diseases such as hypertension and diabetes, and increase the risk of psychiatric symptoms such as depression and anxiety, not to cause subjective distress [16,17]. Many sleep disorders go undetected and are not appropriately treated in clinical practice. Therefore, this study was conducted to alert practitioners of sleep disorders to this situation, by shedding more light on their current status in general medical practice.

In the present study, we investigated the prevalence of sleep disorders and the use of hypnotic-sedative drugs in 421 inpatients with mean age of 72.5 years by questionnaire-, actigraph- and observation-based sleep evaluations, and have revealed a high prevalence of diverse types of sleep disorders

in the study population. SAS, RLS, PLMD, NBD and insomnia, in particular, were highly prevalent (10.0, 5.9, 4.0, 6.9 and 62.7%, respectively). The inpatients also suffered from various sleep-related symptoms (1.0–6.9%, except for sleep paralysis), which are common conditions with physical disorders and which could cause disrupted sleep [18–21]. In fact, the patients with these sleep disorders also showed poor sleep parameters recorded by actigraphy, which objectively indicates that they have poor-quality sleep during the night. Consequently, of the 421 patients, only 13.8% were free of any type of sleep disorder diagnosed, severe daytime sleepiness or sleep-related symptoms, revealing that sleep-related problems are very common clinical problems among inpatients of acute hospital wards.

Due to restrictions on the disclosure of personal information, the only information available regarding the underlying diseases of the patients was the names of the primary diseases according to the major classification of the *ICD-10*. We were thus unable to analyze respective medical conditions that are commonly associated with these sleep disorders, such as chronic pain, cardiovascular diseases, chronic renal failure, hemodialysis and iron deficiency anemia.

The prevalence of SAS and RLS is generally high in elderly people and patients with physical disorders. However, even though the mean age of our patients was high (72.5 years) and they had physical disorders in the exacerbation phase, contrary to our expectations, the prevalence of SAS and RLS was not higher in the study population than in community dwellers of previous studies. For example, the prevalence of SAS in middle-aged to elderly people has been shown to be 9–10% in males and 4–10% in females [22,23], which is comparable to that in the present study population (10% in the entire population, 12.7% in males, 6.7% in females). In the present study, patients were defined as having SAS if they reported loud snoring or apnea lasting for 10 seconds or more, because loud snoring is the most prominent symptom of upper airway resistance syndrome, which is included in the category of SAS [7,24]. Nevertheless, the prevalence of SAS patients including those who snored loudly in the present study was similar to that in the general population. Similarly, a large-scale survey which employed a self-administered questionnaire and used a definition of RLS similar to that in the present study has reported that the prevalence of RLS among Japanese people aged 70 years or more is 4.1% (3.4% in males, 4.6% in females), which is practically identical to that in the present study (5.9% in total, 6.1% in males, 5.7% in females) [25]. Furthermore, the frequency of NBD was as low as 6.9%, despite the occurrence rate of delirium per admission varying between 11 and 42% [26]. The low NBD frequency of the present study compared to that of all previous studies is thought to be because patients with severe physical conditions or with organic brain damages were excluded from the analyses.

In many of the epidemiologic studies on the prevalence of sleep disorders, sleep evaluation is performed during a period of one week to one month. The fact that sleep evaluation in this study was performed on a single night might have held down the prevalence of sleep disorders. However, since the physical status of the inpatients of acute hospital wards can change in a very short period of time and their sleep condition is also subject to change, we assumed that the results obtained from a long investigation period would not properly reflect the actual status of their sleep-related problems. Extension of the duration for determining the presence or absence of sleep disorders may result in a dramatic increase in the prevalence of the sleep disorders in inpatients of acute hospital wards.

Patients with physical disorders, especially with advanced age, are generally vulnerable to insomnia [27–29]. We have found that approximately two thirds (62.7%) of the representative patients in acute wards in Japan are suffering from insomnia. It was confirmed not only from the subjective complaints of patients but also from the objective sleep evaluation that the quality of sleep for patients with insomnia receiving no treatment or who had other sleep disorders was significantly lower than that for patients in the GS group (Table 3). A survey among 1500 community dwellers aged 55–84 years in the United States has demonstrated that the quality of sleep decreases in proportion to an increase in the number of physical disorders suffered [27]. Several studies have also reported a high prevalence (34–69%) of insomnia in outpatients of primary care clinics or regular inpatients with acute or chronic physical disorders [30–33]. The findings of the present study for acute ward inpatients are consistent with those obtained in the previous studies in spite of shorter-term sleep evaluation.

In many cases of sleep disorders, daytime sleepiness often occurs to compensate for low-quality sleep during the night. In the present study, 47.5% of the patients experienced mild or severer sleepiness and 6.9% experienced severe sleepiness, which was particularly high in those with multiple sleep disorders, including SAS, RLS, PLMD and NBD. The results of multiple logistic regression analysis indicated that severe sleepiness is significantly associated with SAS and PLMD, and not with an underlying disease or type of hypnotic-sedative drug.

Only one-third (33.7%) of the patients with insomnia included in the present investigation received treatment for insomnia symptoms. In addition, two-thirds (65.2%) of the patients receiving medication therapy complained of residual insomnia symptoms. The relatively low frequency of patients prescribed hypnotic-sedative drugs in the present study, which is very similar to that reported in the Meissner's study [30], suggests the possibility that physicians are not fully aware of the presence of insomnia in their patients.

The prescribed drugs mainly consisted of benzodiazepine hypnotics including intermediate-acting agents and antipsychotics. Caution should always be exercised when

using these hypnotic-sedative drugs in inpatients with physical disorders, especially in elderly patients. This is because elderly patients present a poor risk-benefit balance for hypnotic-sedative drugs due to such reasons as decreased drug metabolizing capacity, increased drug sensitivity, risk of fall and fracture or suppressed mental function, and worsening of underlying diseases induced by medication [34–37].

Moreover, administered hypnotic-sedative drugs may be ineffective or even worsen underlying diseases unless sleep disorders are properly diagnosed. In fact, 23.8% of the patients with SAS were prescribed hypnotic-sedative drugs including benzodiazepines and 36.0% of the patients with RLS were taking hypnotic-sedative drugs other than clonazepam. These results suggest that medications that are not necessarily appropriate for treatment of individual patients' sleep disorders are often selected in actual clinical practice, possibly causing a reduction in the patients' ADL and QOL.

Several limitations should be noted when interpreting the results of the present study. First, as elderly patients aged 65 years or more accounted for a large portion (76.0%) of the 421 inpatients, it is speculated that the high prevalence of sleep-related problems observed in the patients of the present investigation were associated with not only sleep disorders attributable to physical disorders but also age-related changes in sleep property.

Second, one-fourth (24.4%) of the initially enrolled 557 patients were excluded. Patients who were unable to answer questions on the day of the survey because of a change in their physical condition (e.g. fever, consciousness disturbance or need for emergency examination) or those patients with missing data due to interruptions in LC data collection were excluded. Some of these excluded patients might have developed some type of sleep disorder during their stay in hospital.

Third, insomnia defined in the present study is different from insomnia that meets the general criteria of the International Classification of Sleep Disorders, second edition (ICSD-2) [7], because we did not consider the presence or absence of "daytime impairment related to the nighttime sleep difficulty". This investigation item was not included in the present study because it was difficult to determine whether the patients' diverse psychosomatic symptoms observed during the daytime were attributable to insomnia or physical disorders.

Fourth, the questionnaire employed in the present study has not been validated. A set number of items taken from the original were configured so as to reduce the burden on inpatients who were in poor physical condition. Therefore, the questionnaire can only suggest the possibility of certain disorders such as SAS, PLMD and RLS; it does not predict the presence of these disorders with high accuracy. However, the frequency of sleep disorders and the percentage of patients exhibiting symptoms of insomnia found in the present study closely resemble the data of several other studies. This is thought to be indirect evidence that, to a certain degree, the survey items work effectively to detect patients suffering from sleep disorders.

Fifth, the sleep/wake scoring algorithm used for the LC data in the present study has been validated for a sample of healthy young subjects [15], but not for elderly subjects with physical disorders, as in the present study's sample. However, as the results demonstrate, meaningful differences were detected in the sleep parameters calculated with this algorithm for total sleep time, total wake time, and efficiency of sleep between the UT group with insomnia and the GS group. Given this, the clinical application of the LC and sleep/wake scoring algorithm for the subjects of the present study can be considered a sound approach to a certain degree.

5. Conclusion

In the present study, which initially involved 557 inpatients who had been admitted to acute hospital wards in 44 general hospitals, we have revealed an extremely high prevalence of sleep disorders using subjective and objective sleep evaluation scales, and have also indicated several problems in the current practice of sleep medicine. Proper diagnosis of sleep disorders should be made while being aware of the high prevalence of sleep disorders among elderly patients with physical disorders, and a treatment strategy that provides a favorable risk-benefit balance must be developed.

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References

[1] Manabe K, Matsui T, Yamaya M, Sato-Nakagawa T, Okamura N, Arai H, et al. Sleep patterns and mortality among elderly patients in a geriatric hospital. Gerontology 2000;46:318–22.
[2] Wolkove N, Elkholy O, Baltzan M, Palayew M. Sleep and aging: 1. Sleep disorders commonly found in older people. CMAJ 2007;176: 1299–304.
[3] Bixler EO, Kales A, Soldatos CR, Kales JD, Healey S. Prevalence of sleep disorders in the Los Angeles metropolitan area. Am J Psychiatry 1979;136:1257–62.
[4] Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention. JAMA 1989; 262:1479–84.
[5] Kim K, Uchiyama M, Okawa M, Liu X, Ogihara R. An epidemiological study of insomnia among the Japanese general population. Sleep 2000;23:41–7.
[6] Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6:97–111.

[7] American Acdemy of SleepMedicine. International classification of sleep disorders :Diagnostic and coding manual. 2nd ed. Westchester: Illinois; 2005.
[8] Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378–84.
[9] Javaheri S, Parker TJ, Liming JD, Corbett WS, Nishiyama H, Wexler L, et al. Sleep apnea in 81 ambulatory male patients with stable heart failure. Types and their prevalences, consequences, and presentations. Circulation 1998;97:2154–9.
[10] Oldenburg O, Lamp B, Faber L, Teschler H, Horstkotte D, Topfer V. Sleep-disordered breathing in patients with symptomatic heart failure: a contemporary study of prevalence in and characteristics of 700 patients. Eur J Heart Fail 2007;9:251–7.
[11] Hui DS, Wong TY, Li TS, Ko FW, Choy DK, Szeto CC, et al. Prevalence of sleep disturbances in Chinese patients with end stage renal failure on maintenance hemodialysis. Med Sci Monit 2002;8:CR331–6.
[12] Allen RP, Earley CJ. Restless legs syndrome: a review of clinical and pathophysiologic features. J Clin Neurophysiol 2001;18:128–47.
[13] Nomura T, Inoue Y, Miyake M, Yasui K, Nakashima K. Prevalence and clinical characteristics of restless legs syndrome in Japanese patients with Parkinson's disease. Mov Disord 2006;21:380–4.
[14] Hanly P, Powles P. Hypnotics should never be used in patients with sleep apnea. J Psychosom Res 1993;37(Suppl 1):59–65.
[15] Enomoto M, Eudo T, Suenaga K, Miura N, Nakano Y, Kohtoh S, et al. Newly developed waist actigraphy and its sleep/wake scoring algorithm. Sleep Biol Rhythms 2009;7:17–22.
[16] Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165:1217–39.
[17] Sivertsen B, Krokstad S, Overland S, Mykletun A. The epidemiology of insomnia: associations with physical and mental health. The HUNT-2 study. J Psychosom Res 2009;67:109–16.
[18] Ulloa EW, Salup R, Patterson SG, Jacobsen PB. Relationship between hot flashes and distress in men receiving androgen deprivation therapy for prostate cancer. Psychooncology 2009;18:598–605.
[19] Woodward S, Freedman RR. The thermoregulatory effects of menopausal hot flashes on sleep. Sleep 1994;17:497–501.
[20] Stein MB, Chartier M, Walker JR. Sleep in nondepressed patients with panic disorder: I. Systematic assessment of subjective sleep quality and sleep disturbance. Sleep 1993;16:724–6.
[21] Partinen M. Epidemiology of sleep disorders. In: Kryger M, Roth T, Dement W, editors. Principals and oractice of sleep medicine. 2nd ed. Philadelphia: WB Saunders; 1994. p. 437–52.
[22] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.
[23] Kim J, In K, You S, Kang K, Shim J, Lee S, et al. Prevalence of sleep-disordered breathing in middle-aged Korean men and women. Am J Respir Crit Care Med 2004;170:1108–13.
[24] The Report of an American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep 1999;22:667–89.
[25] Enomoto M, Li L, Aritake S, Nagase Y, Kaji T, Tagaya K, et al. Restless legs syndrome and its correlation with other sleep problems in the general population of Japan. Sleep Biol Rhythms 2006;4:153–9.
[26] Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. Age Ageing 2006;35:350–64.
[27] Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J Psychosom Res 2004;56: 497–502.
[28] Stewart R, Besset A, Bebbington P, Brugha T, Lindesay J, Jenkins R, et al. Insomnia comorbidity and impact and hypnotic use by age group in a national survey population aged 16 to 74 years. Sleep 2006;29: 1391–7.
[29] Taylor DJ, Mallory LJ, Lichstein KL, Durrence HH, Riedel BW, Bush AJ. Comorbidity of chronic insomnia with medical problems. Sleep 2007;30:213–8.
[30] Meissner HH, Riemer A, Santiago SM, Stein M, Goldman MD, Williams AJ. Failure of physician documentation of sleep complaints in hospitalized patients. West J Med 1998;169:146–9.
[31] Shochat T, Umphress J, Israel AG, Ancoli-Israel S. Insomnia in primary care patients. Sleep 1999;22(Suppl 2):S359–65.
[32] Terzano MG, Parrino L, Cirignotta F, Ferini-Strambi L, Gigli G, Rudelli G, et al. Studio Morfeo: insomnia in primary care, a survey conducted on the Italian population. Sleep Med 2004;5: 67–75.
[33] Aikens JE, Rouse ME. Help-seeking for insomnia among adult patients in primary care. J Am Board Fam Pract 2005;18:257–61.
[34] Neutel CI, Perry S, Maxwell C. Medication use and risk of falls. Pharmacoepidemiol Drug Saf 2002;11:97–104.
[35] Mahoney JE, Webb MJ, Gray SL. Zolpidem prescribing and adverse drug reactions in hospitalized general medicine patients at a Veterans Affairs hospital. Am J Geriatr Pharmacother 2004;2:66–74.
[36] Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. BMJ 2005;331:1169.
[37] Chang CM, Wu EC, Chang S, Lin KM. Benzodiazepine and risk of hip fractures in older people: a nested case-control study in Taiwan. Am J Geriatr Psychiatry 2008;16:686–92.

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Regular Article

Relationship between late-life depression and life stressors: Large-scale cross-sectional study of a representative sample of the Japanese general population

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Aim: The purpose of the present study was to clarify the relationship between late-life depression and daily life stress in a representative sample of 10 969 Japanese subjects.

Methods: Data on 10 969 adults aged ≥50 who participated in the Active Survey of Health and Welfare in 2000, were analyzed. The self-administered questionnaire included items on 21 reasons for life stressors and the magnitude of stress, as well as the Japanese version of the Center for Epidemiologic Studies Depression Scale (CES-D). The relationship between the incidence of life stressors and mild–moderate (D_{16}) and severe (D_{26}) depressive symptoms was examined using logistic regression analysis.

Results: A total of 21.9% of subjects had D_{16} symptoms, and 9.3% had D_{26} symptoms. Further, increased age and being female were associated with more severe depressive state. Logistic regression analysis indicated that the strongest relationship between both the incidence of D_{16} and D_{26} symptoms and life stressors stemmed from 'having no one to talk to' (odds ratio = 3.3 and 5.0, respectively). Late-life depression was also associated with 'loss of purpose in life', 'separation/divorce', 'having nothing to do', 'health/illness/care of self', and 'debt'.

Conclusion: There is a relationship between late-life depression and diminished social relationships, experiences involving loss of purpose in life or human relationships, and health problems in the Japanese general population.

Key words: affective disorder, epidemiology, old age psychiatry, public health, stress.

WITH A 12-MONTH prevalence rate of 3–5%[1,2] and a lifetime prevalence rate of 3–20%,[3] depression (major depression) is a highly prevalent and serious disorder with significant clinical and socioeconomic ramifications. Based on the disability-adjusted life year (DALY), a measure developed by the World Health Organization (WHO), depression is projected by the year 2020 to become the second leading burdensome disease following coronary heart disease, imposing a tremendous health burden upon people. Patients with depression experience marked impairments in life functioning and well-being, and are reported to exhibit a reduction in social functioning at a level equivalent to, or more significant than, those living with chronic physical

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illness such as cardiopulmonary disease, arthritis, hypertension, and diabetes.[4,5]

Of the general population aged ≥65, approximately 10–15% are estimated to be depressed and 1–3% are estimated to have major depression.[6,7] Older adults with depression have poor clinical outcomes. In a meta-analysis of 24-month clinical outcomes among the elderly with depression, only 33% were healthy, while 33% remained depressed and 21% had died.[8]

Depression is the most serious psychiatric disorder in late life that is associated with suicide.[9] Results from WHO research investigating the types of psychiatric disorders in suicide victims at the time of their death using techniques such as psychological autopsy indicate that approximately 30% of suicide victims had a mood disorder.[10] The total number of suicides in Japan, which is known for its high suicide rate, exceeded 30 000 in 2007; 36.6% and 21.3% of the suicide victims were people aged ≥60 and those in their 50s, respectively. Therefore, nearly 60% of all suicides were committed by individuals in late life, that is, people aged ≥50 (42% of the population at the time). Thus, improvement of mental health among people in late life is considered to be medically urgent in order to prevent an increase in suicides in a progressively aging society.

The entire clinical course of a psychiatric disorder – from onset to recovery – is affected by biological, psychosocial, and environmental factors in a complex manner. Although psychiatric symptoms are largely determined by biological factors, their clinical outcomes are exacerbated by psychosocial stress.[11] Risk factors for depression identified in research include neurotransmitter abnormalities, sleep disorders, hormone imbalance, substance use, premorbid personality, and stressful life events.[12–14] Stressors that may trigger depression, such as decreased physical and mental functioning due to aging, high prevalence of physical illness, hospitalization, and changes in living environment (e.g. retirement, living alone), are especially salient in late life. Risk factors for the incidence and recurrence of late-life depression have been found to include impairments due to physical illness, fatigue of caregiving, and psychosocial stress such as bereavement and social isolation.[15] Although these insights suggest that psychological stress plays an important role in late-life depression, this has not yet been investigated in a large-scale study using a representative sample of the Japanese general population. The aim of the present study was therefore to clarify the relationship between the incidence of psychosocial stress in daily life (life stressors) and depressive symptoms among more than 10 000 late-life adults selected from 300 communities in Japan.

METHODS

Subjects

The present study was conducted as part of the Active Survey of Health and Welfare (ASHW), a nationwide survey on sleep, mood, stress, and related coping behaviors conducted by the Japanese Ministry of Health, Labour and Welfare in June 2000. The purpose of the ASHW, which was conducted in 1996, 1997, 1999, and 2000, was to provide data to aid the Government's health and welfare policy making. To ensure that the sample was representative of the general population, survey participants were selected among individuals aged ≥12 living in 300 communities in Japan. These communities were selected from 881 851 precincts identified in the 2000 Census using a stratified sampling design. In each community, a part-time investigator employed by the local public health center delivered the self-administered questionnaire to the participants and collected the completed questionnaires a few days later. Oral informed consent was obtained from all subjects.

Table 1 lists the age distribution and male : female ratio of the final study sample with corresponding statistics calculated from the Census data from the same year.

Procedures

The self-administered questionnaire included items concerning sociodemographic characteristics such as age, sex, and community size, and items concerning life stress. In addition, depressive symptoms were assessed using the Japanese version of the Center for Epidemiologic Studies Depression Scale (CES-D).[16,17]

The life stressors were assessed with the question: 'What types of troubles, hardships, stress, or dissatisfaction with daily life did you experience during the past month? Please select all that apply'. The questionnaire was designed to ask participants to mark items only when they identified them as stressors, rather than simply asking about the presence of stressors. The list included a total of 21 choices subsumed under five domains: (i) problems with

Table 1. Subject characteristics (n = 10 969) vs 2000 Census data

Age group (years)	Present study				Census (2000)			(thousand)
	Total (%)	Female (%)	Male (%)	M/F	Total (%)	Female (%)	Male (%)	M/F
50–59	5 036 (45.9)	2583 (44.3)	2453 (47.7)	0.95	19 176 (39.2)	9 676 (36.6)	9 500 (42.3)	0.98
60–69	3 436 (31.3)	1745 (30.0)	1691 (32.9)	0.97	14 841 (30.3)	7 735 (29.2)	7 107 (31.6)	0.92
70–79	1 802 (16.4)	1003 (17.2)	799 (15.5)	0.80	10 051 (20.5)	5 755 (21.8)	4 296 (19.1)	0.75
80–	695 (6.3)	495 (8.5)	200 (3.9)	0.40	4 848 (9.9)	3 279 (12.4)	1 569 (7.0)	0.48
Total	10 969 (100.0)	5826 (100.0)	5143 (100.0)	0.88	48 917 (100.0)	26 445 (100.0)	22 472 (100.0)	0.85

primary support group (separation/divorce; health/illness/care of self; death of a close person; burden of housework; family relationship; relationship with relatives; and health/illness/care of family); (ii) problems related to social environment (having no one to talk to; loss of purpose in life; having nothing to do; and retirement); (iii) occupational problems (commuting [crowded public transportation, long distance etc.]; workplace relationship; unemployment; adjusting to a new job; stress on the job); (iv) housing problems (relationship with neighbors; living environment [pollution, noise etc.]; concerns about housing); and (v) financial problems (debt; and income/household budget). The strength (burden) of life stressors was assessed with the question: 'Have your troubles, hardships, stress, or dissatisfaction with daily life interfered with your social life or everyday life during the past month?' Participants answered this question on a 4-point scale: 1, much; 2, some; 3, little; or 4, none.

The CES-D is a 20-item instrument specifically designed to screen for depression among the general population, and in the present study it was used to assess subjective depressive symptoms during the past week. Each item on the CES-D is scored from 0 to 3, yielding a total score ranging from 0 to 60, with higher scores indicating more severe depressive symptoms. A cut-off score of ≥16 may indicate the presence of depression.[16] Almost 30% of Japanese adults reportedly score ≥16 on the CES-D,[18] suggesting an overestimation of the prevalence of depression compared with Japan as a whole, as well as to Western European countries. Therefore, we defined a CES-D score of ≥26 as a cut-off to select subjects whose symptoms more closely approximate those of major depression according to the criterion used by Cho *et al.*[19] As a result, the present study identified the following three groups of subjects based on the severity of depressive state: (i) control group scoring <16 on the CES-D (mean ± SD = 9.5 ± 4.0); (ii) D_{16} group having mild–moderate depressive symptoms with a score of 16–25 on the CES-D (mean ± SD = 19.8 ± 2.8); and (iii) D_{26} group having severe depressive symptoms with a score of ≥26 on the CES-D (mean ± SD = 32.8 ± 6.5).

Statistical analysis

After contrasting our study sample data with the Census data, we adjusted the sample size for gender and age group. The study sample was classified into two gender groups and four age groups in decades (Table 1). For each of these eight subgroups, we weighted the sample size based on the population proportion (weight(i) = percentage of Census population in subgroup(i)/percentage of sample in subgroup(i), where $i = 1, \ldots, 8$).[1] We conducted the following statistical analyses based on the weighted samples.

Mean CES-D scores were compared using two-way (age group × gender) analysis of variance (ANOVA), followed by Bonferroni post-hoc comparisons. Differences in the distribution of subjects in the control, the D_{16}, and the D_{26} groups as well as the male : female ratios were analyzed using the χ^2 test.

We further examined the relationship between the incidence of life stressors and mild–moderate (D_{16}) and severe (D_{26}) depressive symptoms using multiple logistic regression analysis. The following parameters were entered as covariates: life stressors, gender, age group, community size (cities with population of ≥150 000 were coded as metropolis, while those with a population <150 000 were coded as town/village), geographic region (north, east, west, or south), and strength (burden) of life stressors. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Statistical significance was set at 0.05. All analyses were performed using SPSS 11.5 for Windows (SPSS, Chicago, IL, USA).