The prevalence of restless legs syndrome in Taiwanese adults

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Aim: Few studies have examined the prevalence of restless legs syndrome (RLS) in Asian populations, with existing data suggesting substantially lower rates of RLS in Asian populations compared with Caucasians. However, varying definitions of RLS as well as problematic methodology make conclusions about RLS prevalence in Asian populations difficult to interpret. The current study therefore examines the prevalence of RLS in Taiwanese adults.

Methods: Subjects were 4011 Taiwanese residents over the age of 15 years. Data was collected using a computer-assisted telephone interviewing (CATI) system between 25 October 2006 and 6 November 2006.

Results: The prevalence of RLS in Taiwanese adults was found to be 1.57%. In addition, individuals with RLS had a higher body mass index (BMI) and

incidence of chronic conditions and comorbidities including insomnia, hypertension, cardiovascular disease, respiratory disease, arthritis, backache and mental illness. Women with RLS also had a higher incidence of post-menopausal syndrome.

Conclusion: Findings from the current study suggest that the prevalence of RLS in Taiwan is 1.57% by telephone interview. Individuals with RLS had a higher incidence of chronic insomnia and many other chronic disorders. The association and long-term consequences of RLS with these chronic disorders warrants further longitudinal observation and study.

Key words: Asian, prevalence, restless legs syndrome, Taiwan, urge to move.

RESTLESS LEGS SYNDROME (RLS) is a common sensorimotor disorder first described by Willis in 1672.[1] It is characterized by an urge to move, associated with paresthesias, worsening in the evening and

relieved by activity. Ekbom, a Swedish neurologist, estimated that RLS affects 5% of the general population.[2] The widely accepted diagnostic criteria for RLS was developed in 2003,[3] in which the RLS Working Group revised the diagnosed criteria established by the International Restless Legs Syndrome Study Group (IRLSSG) in 1995.[4]

The prevalence of RLS in Western countries is estimated to be 8.5–14.2% of the general population.[5–14] Some studies have suggested that RLS prevalence doubles in women and with increasing age.[7–9] However, reports of RLS prevalence in Asian

populations have been rare and the results have been highly variable. Most studies show a substantially lower prevalence (0.1% to 4%) of RLS in Asian populations compared to Caucasian populations.[15–21] Furthermore, the majority of these studies have problematic methodology and inconsistent definitions of RLS, which preclude a prevalence consensus. In order to understand the prevalence of RLS in the Asian population, a crucial study was designed according to the current definition of RLS with a valid methodology and that study served as the impetus for the current study.[4]
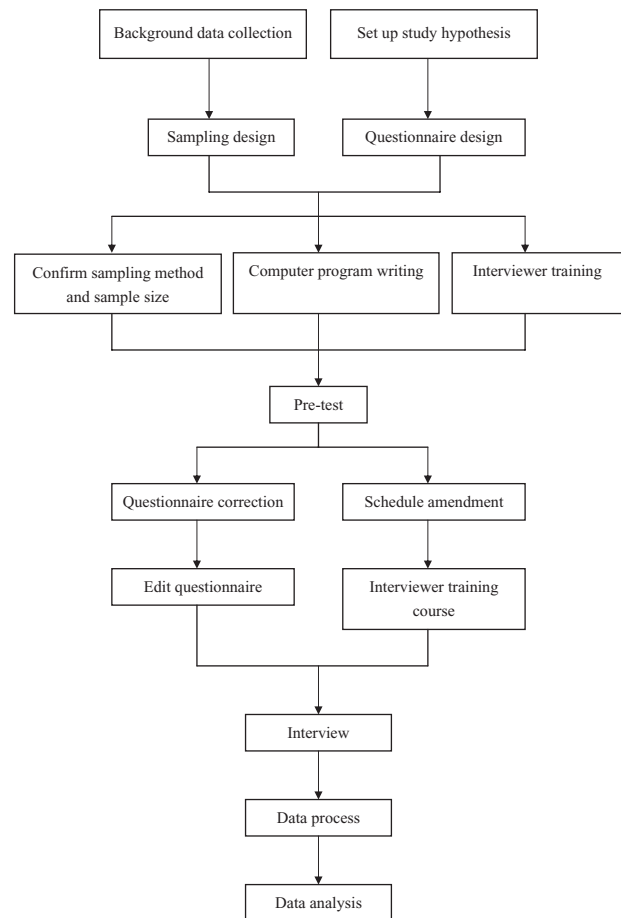
METHODS

Subjects

The subjects were residents over the age of 15 years currently residing in Taiwan. The number of subjects to be interviewed was calculated according to the estimated prevalence in previous reports and the population distributions in each county. From 25 October 2006 to 6 November 2006, 11 649 individuals selected randomly from Taiwan's national telephone directory were approached using a computer-assisted telephone interviewing system (CATI).[22] A total of 3862 (33.2%) subjects refused to be interviewed for any reason, and 3776 (32.4%) subjects did not complete the interview due to problems such as language barriers, hearing impairment, communication difficulty and poor telephone/cell phone quality. In total, 4011 (34.4%) participants successfully completed the interview during the investigational period. This number reached the requirement of a 95% confidence interval (CI) and bias of 3%.

Pre-survey procedures and the survey system – CATI system

Pre-survey procedures are presented in Figure 1 and included setting up the study hypothesis, collecting background data, designing the sampling method, preparation and validation of the questionnaires, and translation and back translation of the essential diagnostic criteria into the questionnaires. Thirty subjects were included for validation of the questionnaire with a Kappa of 0.67. Following question validation, the computer program was developed and revised according to the study protocol. A training course for

Figure 1. Procedure of the Taiwan restless legs syndrome study.

all interviewers was provided to introduce the background of the study and the operation of the CATI system.

The CATI system is a well-established method of conducting telephone-based interviews with the assistance of a computer. This popular methodology involves a telephone interviewer reading from a computer-based questionnaire and typing in the responses as they are reported. Advantages of the CATI system include standardization of investigator protocols across multiple users and reduction of data errors through the use of integrated data management tools for report generation and analysis. The precise operation of CATI in the current study is similar to other population-based studies and is detailed in the first supplement (see Supplementary Data 1).[22,23] Individual telephone numbers were

selected randomly from Taiwan's national telephone directory and were dialed digitally. Oral informed consent was obtained before starting the procedure. Participants were interviewed by 40 well-trained telephone investigators.

Primary study questions

Questions at the prompts during the telephone interview enabled the collection of data for RLS and chronic insomnia symptoms, major medical conditions and demographic information. Demographic data such as gender, age, body mass index (BMI), and marital status were also obtained. Questions regarding RLS, asked according to the criteria set by the International Restless Legs Syndrome Study Group, were used as follows:

1 Over the past month, have you had any uncomfortable sensations or an urge to move your legs at rest?
2 Over the past month, did the uncomfortable sensations or urge to move your legs occur or exacerbate when you were sitting or lying down?
3 Over the past month, were the uncomfortable sensations or urge to move your legs relieved by movement, for example, walking around?
4 Over the past month, did the uncomfortable sensations or urge to move the legs worsen during the evening or night when compared with the daytime?

Questions regarding chronic insomnia included the following:

1 Did you have difficulty falling asleep, more than 4 days per week, lasting at least one month?
2 Did you have difficulty staying or returning to sleep when you woke up at night, more than 4 days a week, lasting at least one month?
3 Did you wake up earlier than you expected, more than 4 days a week, lasting at least one month?
4 Did you still feel tired, even after a whole night of sleep, more than 4 days a week, lasting at least one month?

Questions also addressed the occurrence of major medical diseases in the past year, such as hypertension (defined as a diagnosis of hypertension established by a physician or being under treatment for hypertension), cardiovascular disease (defined as

angina or myocardial infarction or heart attack reported by a physician), diabetes mellitus (defined as a diagnosis established by a physician), arthritis, backache, respiratory disease (such as chronic bronchitis, asthma, or emphysema), anemia, mental disease (such as depression, anxiety, or bipolar disorder established by a psychiatric physician), postmenopausal syndrome or chronic renal failure under hemodialysis. The final questionnaire for CATI is included in the supplementary data (Supplementary Data 2).

Statistical analysis

The χ^2-test was applied to compare categorical data and independent-samples. *T*-tests were applied to compare the mean value of two groups. Logistic regression was used to test the relationship and determine the odds ratio (OR) of RLS with age, gender, BMI, chronic insomnia, chronic disorders, and some demographic data. All statistical tests utilized SAS software (SAS Institute, Cary, NC, USA) and a value of $P < 0.05$ for statistical significance.

RESULTS

A total of 4011 Taiwanese adults, including 1634 male subjects (40.7%) and 2377 female subjects (59.3%), were interviewed successfully. The average age was 47.7 ± 16.6 years old. The mean BMI of the entire sample was 23.0 ± 3.5. The majority of the sample was married (72.6%) and 51.4% worked full- or part-time. Twenty-five percent of the sample remained at home and 12.3% were retired.

The prevalence of RLS in individuals 15–70 years of age within the Taiwanese population is presented in Table 1. A total of 1.57% of the sample endorsed

Table 1. Prevalence of restless legs syndrome (RLS) with the four criteria in Taiwanese adults ($n = 4011$)

	Number	Percentage
Meet all 4 RLS criteria	63	1.57%
Meet 3 criteria[†]	180	4.49%
Meet 2 criteria[‡]	335	8.35%

[†]Meet 3 criteria means subjects have the urge-to-move sensation with another 2 criteria.
[‡]Meet 2 criteria means subjects have the urge-to-move sensation with another one criterion.
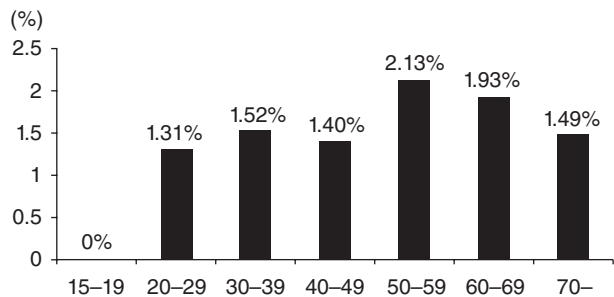
Figure 2. Prevalence distribution of age group in Taiwan restless legs syndrome study.

all four criteria for RLS. In addition, 4.49% of participants endorsed the sensation of an urge to move with at least two other criteria for RLS. Lastly, 8.35% endorsed the sensation of an urge to move with at least one other criterion for RLS. The distribution of RLS across the different age groups is shown in Figure 2. Individuals between 50 and 59 years of age experienced the highest incidence (2.13%) of RLS in Taiwan.

Table 2 presents the demographic data of subjects who met all four RLS criteria (diagnosis of RLS) and comparisons with subjects without any complaints of RLS. Age and marital status were not significantly different between the two groups. Female participants tended to have a higher prevalence of RLS but this did not reach statistical significance. The RLS group had a significantly higher mean BMI than the group without RLS symptoms ($P = 0.014$).

Taiwanese adults with RLS had a higher incidence of chronic insomnia when compared to the normal population in our study (31.75% vs 11.5%, $P < 0.05$, Fig. 3a). Furthermore, all chronic insomnia symp-

toms including 'difficulty falling asleep', 'difficulty staying asleep', 'waking up earlier' and 'non-refreshing sleep' were higher in the RLS population compared with those of the normal study population (20.63% vs 7.80%, 11.11% vs 3.77%, 12.70% vs 4.03% and 15.87% vs 4.89%, respectively, $P < 0.05$, Fig. 3b). The incidence of RLS (4.13%) in subjects with chronic insomnia was higher than that in the subjects without symptoms of chronic insomnia (1.22%). A total of 12.2% of participants endorsing chronic insomnia experienced at least three symptoms of RLS, whereas 17.2% experienced at least two symptoms. The incidence of hypertension in the RLS population was significantly higher than that of the normal study population ($P < 0.05$). The incidence of cardiovascular disease was 22.2% among RLS subjects, which was also higher than that of subjects without RLS symptoms. The incidence of arthritis, backache, respiratory disease, and mental illness among RLS subjects was 36.5%, 66.7%, 20.6%, and 7.9%, respectively, all of which were significantly higher than those without RLS symptoms ($P < 0.05$, Fig. 4). The incidence of diabetes mellitus, anemia and subjects undergoing hemodialysis were similar between groups (Fig. 4). Women who have RLS also suffered a higher incidence of postmenopausal symptoms (26.3%) than those without RLS (10.8%) ($P < 0.05$, Fig. 5).

A logistic regression model adjusted for age, sex and BMI was utilized to determine odds ratio (OR) for various comorbidities associated with RLS (see Table 3). Any sleep complaints (OR = 11.66, $P = 0.048$) and working style factors (shift work vs day work, OR = 2.57, $P = 0.032$) were identified as significant risk factors for RLS. Individuals with hypertension, cardiovascular disease, arthritis, back

Table 2. Demographic data of subjects who met all four restless legs syndrome (RLS) criteria and subjects without any criteria

	RLS (4 criteria)	Free of RLS symptoms	*P*-value
Gender (M/F)	25/38	1489/2183	$P = 0.891$
Age, average	50.7 ± 14.6	47.7 ± 16.5	$P = 0.204$
Male	51.8 ± 17.2	47.9 ± 18.1	
Female	50.0 ± 12.7	47.5 ± 15.4	
Marital status, single	6 (9.5%)	727 (19.8%)	$P = 0.226$
Married	51 (80.9%)	2679 (72.9%)	
Divorce	2 (3.2%)	80 (2.2%)	
Widow/widower	4 (6.4%)	186 (5.1%)	
Body mass index	24.1 ± 3.3	23.0 ± 3.4	$P = 0.014$

Data present as Mean ± SD.
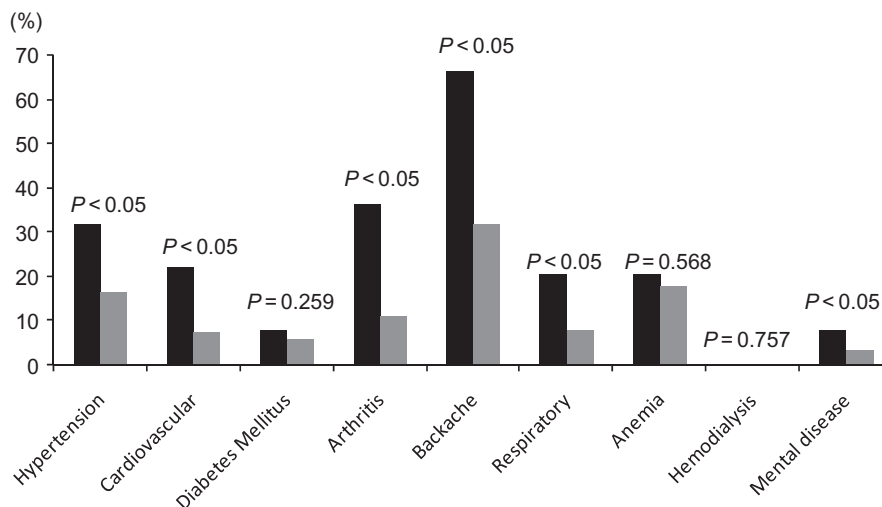
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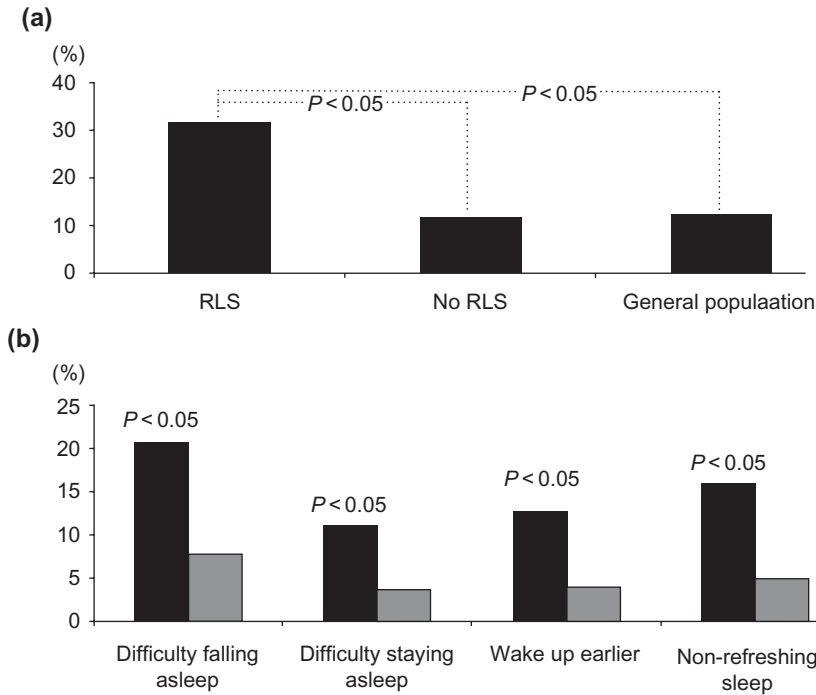
Figure 3. The (a) prevalence and (b) symptoms of chronic insomnia in (■) restless legs syndrome (RLS) versus (▨) no RLS.

pain and respiratory disease and urinary tract disease were also more likely to endorse RLS. Taken together, all comorbidities increased the odds of RLS by 9.46 ($P = 0.003$).
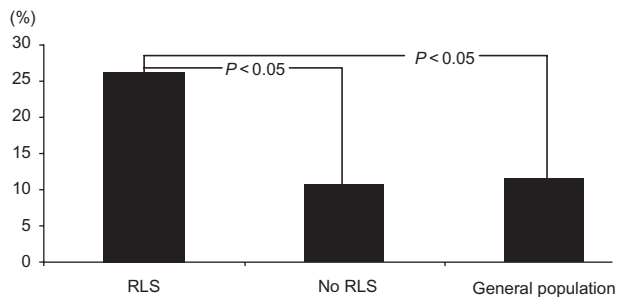
DISCUSSION

Previous reports on the prevalence of RLS in Asian populations are controversial due to inconsistencies in diagnostic criteria. In 2003, the International RLS Study Group/National Institutes of Health formally established criteria for the diagnosis of RLS that have been used in subsequent studies of RLS prevalence.[4] The established prevalence of RLS in Western countries is 8.5–14.2%, establishing RLS as one of the most common movement disorders.[5–10,24,25] However, few studies have examined the prevalence of RLS in Asian populations and results have been

Figure 4. The prevalence of chronic disorders in (■) restless legs syndrome (RLS) versus (▨) no RLS.

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Figure 5. The prevalence of postmenopausal syndrome in women with restless legs syndrome (RLS) versus no RLS.

unexpectedly low in the reports.[10–15] In our study, the prevalence of RLS in patients who met all four diagnostic criteria was 1.57%. Previous reports from Asian countries have varied from 0.1% to 12.1%. However, the methodology utilized in these studies was questionable with extreme reports such as 12.1% reported with only one question used to diagnose RLS or 0.1% in another report with a significant selection bias.[15,17] Other well-designed studies from Asian populations have estimated prevalence rates between 2.1% and 3.9% in Japan, Korea, India and Turkey.[19–21,25] Low prevalence rates have also been documented in older Asian populations (1.06%)[16] and in Asians with chronic conditions such as Parkinson's disease (12.1%).[18] In all of these reports from Asian populations, including our report, the prevalence of RLS is consistently much lower than reports from Caucasian populations. With mounting evidence of a genetic explanation for RLS, it is reasonable to postulate different genetic determinants of RLS for Asians and Caucasians.[26–28]

In our study, participants with RLS were at significantly increased risk for other chronic conditions.

This finding is consistent with other studies documenting associations between RLS and certain disorders. For example, hypertension, cardiovascular disease, arthritis, backache, and respiratory disease were higher in participants with RLS in our study. Similarly, as part of the Wisconsin Cohort study, Winkelman *et al.* reported a high incidence of hypertension and cardiovascular disease in individuals with RLS.[11] Strong associations between RLS and coronary artery disease (OR: 2.05; 95%CI 1.38–3.04) and cardiovascular disease (OR: 2.07, 95%CI 1.43–3.00) were also found in a Sleep Heart Health Study and a Swedish RLS study.[29,30] The association was also noted in our study with an OR of 3.695 and 2.424 for hypertension and cardiovascular disease, respectively. A review by Walters examined possible mechanisms underlying the association between cardiovascular disease and RLS. In this review, sympathetic hyperactivity is noted in patients with RLS during sleep. Insufficient inhibition of sympathetic preganglionic neurons in the spinal cord may be the mechanism predisposing the patient to this sympathetic hyperactivity. Walters suggested that sympathetic hyperactivity may direct injury to the heart or brain, or might be indirectly mediated by hypertension associated with RLS.[31] Taken together, these findings warrant further longitudinal observation and study of the association between RLS and cardiovascular disorders.

Many chronic conditions could coexist with RLS. Lamberg, in his review, suggested that when sharing the same disturbances of sleep in RLS patients, chronic disorders such as backache and arthritis could coexist, as found in our participants.[32] Musculoskeletal diseases or back pain were also found to be associated with RLS in Ohyon's survey and the RLS

Table 3. Adjusted odds ratio of the comorbidities in restless legs syndrome (RLS)

Outcomes	Odds ratio	95% confidence interval	*P*-value
Hypertension	2.424	(1.417, 4.149)	0.0012
Cardiovascular disease	3.695	(2.013, 6.783)	<0.0001
Diabetes mellitus	1.424	(0.566, 3.586)	0.4530
Arthritis	5.163	(3.038, 8.774)	<0.0001
Back pain	4.453	(2.626, 7.552)	<0.0001
Respiratory disease	3.305	(1.774, 6.155)	0.0002
Anemia	1.196	(0.646, 2.214)	0.6179
Mental illness	2.578	(1.015, 6.543)	0.0389
Chronic insomnia	3.492	(2.037, 5.988)	<0.0001

RLS versus non-RLS.

epidemiology, symptoms, and treatment (REST) study by Henning *et al.*[7,12] Mental illness was significantly associated with RLS is our study. A similar finding was reported in Wisconsin's sleep cohort study, in the REST study, as well as studies in Turkey and Scandinavian countries. Anxiety, depression or increased psychotropic medication were significantly associated with RLS in these reports.[7,11–13,19,30,33]

Although rarely reported, women with RLS showed a higher incidence of postmenopausal syndrome in our study.[34] The incidence of two well-known risk factors of RLS, anemia and end-stage renal disease, was not higher in our study. This finding is similar to a study conducted by Hogl *et al.* in Italy.[14] However, the official diagnosis of these two conditions would require confirmation by laboratory tests, which were not conducted as part of either study. Therefore, these findings should be interpreted with some caution. Furthermore, due to the low prevalence of these two diseases in the general population, they may not have been accurately sampled in our survey. Only one responder in our survey endorsed renal failure.

The BMI of individuals with RLS in our study was significantly higher. Obesity or higher BMI have also been associated with RLS in previous studies.[7,11,12] As a risk factor of another prevalent sleep disorder, sleep apnea syndrome, the association of obesity could facilitate the occurrence of sleep apnea syndrome in RLS. Obesity could also be associated with other comorbidities of RLS such as cardiovascular or musculoskeletal diseases.

RLS is frequently underestimated as a primary cause of chronic insomnia. A total of 4.3% of chronic insomniac patients in our study experienced all the symptoms of RLS and 17.2% experienced at least two symptoms of RLS. As the symptoms of RLS are subtle and difficult to define, we believe that even more patients presenting with insomnia complaints may actually be suffering from the symptoms of RLS. These findings highlight the clinical importance of determining the primary etiology of insomnia symptoms in adult patients so that appropriate treatment is provided.

Patients with RLS also have a high incidence (31.85%) of presenting with the symptoms of chronic insomnia according to the definition of the DSM-IV. Although the symptoms of RLS only bother patients before sleep, all four symptoms of insomnia including difficulty initiating sleep, maintaining sleep, early morning awakening and non-restorative sleep were found at increased rates in the RLS popu-

lation. While RLS symptoms may account for increased rates of sleep initiation problems, they do not explain the increased prevalence of sleep maintenance problems seen in our study. It is possible that these individuals may also have periodic limb movement disorder, which frequently coexists with RLS and interferes with the continuity of sleep.

The association of RLS with many chronic diseases is striking and highlights the importance of appropriate diagnosis and treatment of RLS. Because of the association with many chronic health conditions, the social impact of RLS is considerably significant. As mentioned in Henning's reports, patients with RLS consult specialists across many disciplines. In fact, vascular surgeons, rheumatologists and cardiologists rank above neuropsychiatrists and sleep medicine specialists for RLS-related consultations.[12] It is therefore important to broadly educate physicians as well as the general population in the recognition and prevalence of this syndrome.

Questionnaires, personal interviewing and telephone interviewing have been successfully used in previous prevalence studies. More specifically, telephone interviewing was also successfully used in previous studies of RLS prevalence.[7,18,35] The Centers for Disease Control have also used this method for their Behavioral Risk Factor Surveillance System (BRFSS) in order to track health conditions and risk behaviors across the USA yearly since 1984. Fox *et al.* used CATI techniques in an outbreak of cryptosporidiosis and concluded that the CATI method may be maximally applicable in large-scale investigations.[36] The CATI has the added benefits of increasing a researcher's ability to approach more subjects when compared with face-to-face interviews. Despite the many advantages of using the CATI system, there are some limitations that should be considered. Participants may have difficulty expressing the sensations of RLS over the phone, which may confound the results. Participants experiencing partial or rare symptoms may answer 'no' or 'unknown,' artificially lowering the true prevalence. The refusal rate for this study was high, limiting the generalizability of our findings. However, refusal rates in our study were similar to those in other studies employing similar methodologies and telephone surveys are a well-established and cost-effective method for large-scale prevalence research.

In conclusion, the prevalence of RLS in Taiwanese adults surveyed as part of our study was 1.57%. This finding is substantially lower than prevalence rates

documented in primarily Caucasian samples. Individuals with symptoms of RLS had a higher incidence of many chronic disorders including hypertension, cardiovascular disease and mental illness. The association and long-term consequences of RLS with these chronic disorders warrants further longitudinal observation and study.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Supplementary Data 1. Details of pre-survey procedures and the survey system: Computer-assisted telephone interview (CATI).
Supplementary Data 2. The final questionnaire for computer-assisted telephone interview (CATI).

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